Rooke, A.
10/775679

Seq. Claim 27

FILE 'REGISTRY' ENTERED AT 15:03:15 ON 03 MAR 2005
L1 16 S REDEDEIEW/SQSP

FILE 'CAPLUS' ENTERED AT 15:03:36 ON 03 MAR 2005
L2 21 S L1

L2 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 19 Nov 2004
ACCESSION NUMBER: 2004:995647 CAPLUS
DOCUMENT NUMBER: 141:421046
TITLE: Protein and cDNA sequences of the novel human tumor suppressor genes ASPP (apoptosis stimulating proteins of p53) and therapeutic use
INVENTOR(S): Lu, Xin
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: U.S. Pat. Appl. Publ., 81 pp., Cont.-in-part of U.S. Ser. No. 343,649.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004228866	A1	20041118	US 2004-819095	20040405
WO 2002012325	A2	20020214	WO 2001-GB3524	20010806
WO 2002012325	A3	20030306		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004053262	A1	20040318	US 2003-343649	20030904
PRIORITY APPLN. INFO.:			GB 2000-19018 A	20000804
			GB 2000-29996 A	20001208
			GB 2001-12890 A	20010526
			WO 2001-GB3524 W	20010806
			US 2003-343649 A2	20030904

AB The disclosure relates to the identification of a new member of a family of tumor suppressor genes (apoptosis stimulating proteins of p53, ASPP's) which encode polypeptides capable of modulating the activity of p53, p63 and p73, and polypeptides capable of modulating the activity of a tumor suppressor polypeptide.

IT **795109-26-1P**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; protein and cDNA sequences of novel human tumor suppressor genes ASPP (apoptosis stimulating proteins of p53) and therapeutic use)

L2 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 17 Nov 2004
ACCESSION NUMBER: 2004:979661 CAPLUS
DOCUMENT NUMBER: 142:18208
TITLE: The status, quality, and expansion of the NIH full-length cDNA project: The mammalian gene collection (MGC)
AUTHOR(S): Gerhard, Daniela S.; Wagner, Lukas; Feingold, Elise A.; Shenmen, Carolyn M.; Grouse, Lynette H.; Schuler, Greg; Klein, Steven L.; Old, Susan; Rasooly, Rebekah; Good, Peter; Guyer, Mark; Peck, Allicon M.; Derge, Jeffery G.; Lipman, David; Collins, Francis S.
CORPORATE SOURCE: The MGC Project Team, NIH, USA
SOURCE: Genome Research (2004), 14(10b), 2121-2127
CODEN: GEREFS; ISSN: 1088-9051
PUBLISHER: Cold Spring Harbor Laboratory Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The National Institutes of Health's Mammalian Gene Collection (MGC) project was designed to generate and sequence a publicly accessible cDNA resource containing a complete open reading frame (ORF) for every human and mouse gene. The project initially used a random strategy to select clones from a large number of cDNA libraries from diverse tissues. Candidate clones were chosen based on 5'-EST sequences, and then fully sequenced to high accuracy and analyzed by algorithms developed for this project. Currently, more than 11,000 human and 10,000 mouse genes are represented in MGC by at least one clone with a full ORF. The random selection approach is now reaching a saturation point, and a transition to protocols targeted at the missing transcripts is now required to complete the mouse and human collections. Comparison of the sequence of the MGC clones to reference genome sequences reveals that most cDNA clones are of very high sequence quality, although it is likely that some cDNAs may carry missense variants as a consequence of exptl. artifact, such as PCR, cloning, or reverse transcriptase errors. Recently, a rat cDNA component was added to the project, and ongoing frog (Xenopus) and zebrafish (Danio) cDNA projects were expanded to take advantage of the high-throughput MGC pipeline. The sequence data for the full-length clones from this study have been submitted to GenBank/EMBL/DDBJ under accession nos. BC000001-BC077073. [This abstr record is one of 39 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].
IT **606804-01-7**, GenBank AAH58918
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; status, quality, and expansion of the NIH full-length cDNA project and mammalian gene collection (MGC))

L2 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 10 Sep 2004
ACCESSION NUMBER: 2004:740438 CAPLUS
DOCUMENT NUMBER: 141:258758
TITLE: Human nucleic acid and encoded protein sequences overexpressed in prostatic carcinomas
INVENTOR(S): Hinzmann, Bernd; Dahl, Edgar; Rosenthal, Andre; Hermann, Klaus; Pilarsky, Christian; Specht, Thomas; Schmitt, Armin; Beckmann, Georg; Bruemmendorf, Thomas;

Kinnemann, Henrik; Roepcke, Stefan; Li, Xinzhong; Staub, Eike
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 1607 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004076614	A2	20040910	WO 2004-DE433	20040222
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI, NI, NO				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10309985	A1	20040930	DE 2003-10309985	20030227
DE 10322134	A1	20041223	DE 2003-10322134	20030514
PRIORITY APPLN. INFO.:			DE 2003-10309985 A	20030227
			DE 2003-10322134 A	20030514

AB The invention relates to novel human nucleic acid sequences obtained from prostatic carcinomas and to proteins and peptides coded by said sequences. Over-expression of the nucleic acids was identified by chip anal. and quant. PCR. Differential expression of CD24 is demonstrated by GeneChip technol. and by immunohistochem. These nucleic acids and proteins may be used for the diagnosis and/or treatment of prostatic cancer, in screening assays for modulators of gene expression and/or protein activity, and for the design of antisense oligonucleotides, siRNAs, ribozymes, peptides, aptamers, and antibodies.

IT **753036-25-8**
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; human nucleic acid and encoded protein sequences obtained from prostatic carcinomas)

L2 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 04 Jun 2004
ACCESSION NUMBER: 2004:449884 CAPLUS
DOCUMENT NUMBER: 140:420388
TITLE: Binary prediction tree modeling with many predictors and its uses in clinical and genomic applications
INVENTOR(S): Nevins, Joseph R.; West, Mike; Huang, Andrew T.
PATENT ASSIGNEE(S): Duke University, USA
SOURCE: PCT Int. Appl., 886 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004038376	A2	20040506	WO 2003-XB33946	20031024
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2004038376	A2	20040506	WO 2003-US33946	20031024
WO 2004038376	A3	20040826		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:		
US 2002-420729P	P	20021024
US 2002-421062P	P	20021025
US 2002-421102P	P	20021025
US 2002-424701P	P	20021108
US 2002-424715P	P	20021108
US 2002-424718P	P	20021108
US 2002-425256P	P	20021112
US 2003-448461P	P	20030221
US 2003-448462P	P	20030221
US 2003-457877P	P	20030327
US 2003-458373P	P	20030331
WO 2003-US33946	A	20031024

AB The statistical anal. described and claimed is a predictive statistical tree model that overcomes several problems observed in prior statistical models and regression analyses, while ensuring greater accuracy and predictive capabilities. Although the claimed use of the predictive statistical tree model described herein is directed to the prediction of a disease in individuals, the claimed model can be used for a variety of applications including the prediction of disease states, susceptibility of disease states or any other biol. state of interest, as well as other applicable non-biol. states of interest. This model first screens genes to reduce noise, applies kmeans correlation-based clustering targeting a large number of clusters, and then uses singular value decompns. (SVD) to extract the single dominant factor (principal component) from each cluster. This generates a statistically significant number of cluster-derived singular factors, that are referred to as metagenes, that characterize multiple

patterns of expression of the genes across samples. The strategy aims to extract multiple such patterns while reducing dimension and smoothing out gene-specific noise through the aggregation within clusters. Formal predictive anal. then uses these metagenes in a Bayesian classification tree anal. This generates multiple recursive partitions of the sample into subgroups (the 'leaves' of the classification tree), and assocs. Bayesian predictive probabilities of outcomes with each subgroup. Overall predictions for an individual sample are then generated by averaging predictions, with appropriate wts., across many such tree models. The model includes the use of iterative out-of-sample, cross-validation predictions leaving each sample out of the data set one at a time, refitting the model from the remaining samples and using it to predict the hold-out case. This rigorously tests the predictive value of a model and mirrors the real-world prognostic context where prediction of new cases as they arise is the major goal.

IT **178967-19-6**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; binary prediction tree modeling with many predictors and its uses in clin. and genomic applications)

L2 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 16 Apr 2004
ACCESSION NUMBER: 2004:311088 CAPLUS
DOCUMENT NUMBER: 140:333564
TITLE: Transgenic mice comprising ASPP1 and ASPP2 gene knockouts and their use in diagnosis and treatment of neurodegenerative diseases
INVENTOR(S): Lu, Xin
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, Switz.
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004031776	A2	20040415	WO 2003-GB4258	20031003
WO 2004031776	A3	20040527		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-23187 A 20021007

AB The invention relates to a screening method to determine the susceptibility of
a mammal, preferably a human, to abnormal development of the nervous system and including therapeutic methods and compns. for the treatment of

neurodegenerative conditions which result in abnormal expression of a family of polypeptides which induce the apoptotic function of p53. In particular, it relates to transgenic mice comprising ASPP1 and ASPP2 gene knockouts and their use in diagnosis and treatment of neurodegenerative diseases.

IT **679846-54-9**, Protein (mouse gene ASPP2)
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; transgenic mice comprising ASPP1 and ASPP2 gene knockouts and their use in diagnosis and treatment of neurodegenerative diseases)

L2 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 16 Apr 2004
ACCESSION NUMBER: 2004:311032 CAPLUS
DOCUMENT NUMBER: 140:332473
TITLE: Protein and cDNA sequences of apoptosis inhibitor protein iASPP and use for treating cancer
INVENTOR(S): Lu, Xin; Kuwabara, Patricia; Selwood, David
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, Switz.; Genome Research Limited; UCL Cruciform Limited
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004031229	A2	20040415	WO 2003-GB4296	20031003
WO 2004031229	A3	20040923		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-23193 A 20021007
GB 2003-6261 A 20030319

AB The invention provides protein and cDNA sequences of apoptosis inhibitor protein iASPP cloned from human and Caenorhabditis elegans. The invention relates to a polypeptide, or part thereof, which inhibits the apoptotic activity of the tumor suppressor protein p53 and including screening methods to identify agents which interfere with the activity of said polypeptide.

IT **679518-01-5**
RL: PRP (Properties)
(unclaimed sequence; protein and cDNA sequences of apoptosis inhibitor protein iASPP and use for treating cancer)

L2 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 04 Dec 2003
ACCESSION NUMBER: 2003:942767 CAPLUS
DOCUMENT NUMBER: 140:40262
TITLE: Genes expressed in atherosclerotic tissue and their use in diagnosis and pharmacogenetics
INVENTOR(S): Nevins, Joseph; West, Mike; Goldschmidt, Pascal
PATENT ASSIGNEE(S): Duke University, USA
SOURCE: PCT Int. Appl., 408 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003091391	A2	20031106	WO 2002-XB38221	20021112
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2003091391	A2	20031106	WO 2002-US38221	20021112
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:

US 2002-374547P	P	20020423
US 2002-420784P	P	20021024
US 2002-421043P	P	20021025
US 2002-424680P	P	20021108
WO 2002-US38221	A	20021112

AB Genes whose expression is correlated with an determinant of an atherosclerotic phenotype are provided. Also provided are methods of using the subject atherosclerotic determinant genes in diagnosis and treatment methods, as well as drug screening methods. In addition, reagents and kits thereof that find use in practicing the subject methods are provided. Also provided are methods of determining whether a gene is correlated with a disease phenotype, where correlation is determined using a Bayesian anal. [This abstract record is one of three records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

IT **178967-19-6**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL

(Biological study)
(amino acid sequence; genes expressed in atherosclerotic tissue and their use in diagnosis and pharmacogenetics)

L2 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 24 Nov 2003
ACCESSION NUMBER: 2003:917115 CAPLUS
DOCUMENT NUMBER: 140:104698
TITLE: Rescue of mutants of the tumor suppressor p53 in cancer cells by a designed peptide
AUTHOR(S): Issaeva, Natalia; Friedler, Assaf; Bozko, Przemyslaw; Wiman, Klas G.; Fersht, Alan R.; Selivanova, Galina
CORPORATE SOURCE: Department of Oncology-Pathology, Cancer Center Karolinska, R8:00, Karolinska Institutet, Karolinska Hospital, Stockholm, SE-171 76, Swed.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(23), 13303-13307
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We designed a series of nine-residue peptides that bound to a defined site on the tumor suppressor p53 and stabilized it against denaturation. To test whether the peptides could act as chaperones and rescue the tumor-suppressing function of oncogenic mutants of p53 in living cells, we treated human tumor cells with the fluorescein-labeled peptide Fl-CDB3 (fluorescent derivative of CDB3). Before treatment, the mutant p53 in the cell was predominantly denatured. Fl-CDB3 was taken up into the cytoplasm and nucleus and induced a substantial up-regulation of wild-type p53 protein and representative mutants. The mutants, His-273 and His-175 p53, adopted the active conformation, with a dramatic decrease in the fraction of denatured protein. In all cases, there was p53-dependent induction of expression of the p53 target genes mdm2, gadd45, and p21, accompanied by p53-dependent partial restoration of apoptosis. Fl-CDB3 sensitized cancer cells that carried wild-type p53 to p53-dependent γ-radiation-induced apoptosis. Although Fl-CDB3 did not elicit a full biol. response, it did bind to and rescue p53 in cells and so can serve as a lead for the development of novel drugs for anticancer therapy.
IT **497259-83-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rescue of mutants of tumor suppressor p53 in cancer cells by a designed peptide)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 21 Nov 2003
ACCESSION NUMBER: 2003:913280 CAPLUS
DOCUMENT NUMBER: 139:379453
TITLE: Genes showing altered patterns of expression in multiple sclerosis and their diagnostic and therapeutic uses
INVENTOR(S): Dangond, Fernando; Hwang, Daehee
PATENT ASSIGNEE(S): Brigham and Women's Hospital, Inc., USA
SOURCE: PCT Int. Appl., 148 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003095618	A2	20031120	WO 2003-US14462	20030507
WO 2003095618	A3	20041021		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004018522	A1	20040129	US 2003-430762	20030506
PRIORITY APPLN. INFO.:			US 2002-379284P	P 20020509
			US 2003-430762	A1 20030506

AB The present invention identifies a number of gene markers whose expression is altered in multiple sclerosis (MS). These markers can be used to diagnose or predict MS in subjects, and can be used in the monitoring of therapies. In addition, these genes identify therapeutic targets, the modification of which may prevent MS development or progression. Genes were identified by determination of expression profiling. A large number of genes showing altered patterns of expression were identified, with the most discriminatory genes being those for: phosphatidylinositol transfer protein, inducible nitric oxide synthase, CIC-1 (CLCN1) muscle chloride channel protein, placental bikunin (AMBP), receptor kinase ligand LERK-3/Ephrin-A3, GATA-4, thymopoietin, transcription factor E2f-2, S-adenosylmethionine synthetase, carcinoembryonic antigen, the ret oncogene, a G protein-linked receptor (clone GPCR W), GTP- binding protein RALB, tyrosine kinase Syk, LERK-2/Ephrin-B1, ELK1 tyrosine kinase oncogene, transcription factor SL1, phospholipase C, gastricsin (progastricsin), and the D13S824E locus.

IT **178967-19-6**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; genes showing altered patterns of expression in multiple sclerosis and their diagnostic and therapeutic uses)

L2 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 21 Nov 2003
ACCESSION NUMBER: 2003:913187 CAPLUS
DOCUMENT NUMBER: 139:391336
TITLE: Peptides for modulating tumor suppressor protein expression and/or activity
INVENTOR(S): Fersht, Alan; Friedler, Assaf; Wiman, Klas G.; Selivanova, Galina
PATENT ASSIGNEE(S): Medical Research Council, UK
SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003095484	A2	20031120	WO 2003-GB2008	20030509
WO 2003095484	A3	20040108		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-10746 A 20020510

AB The invention discloses peptides which alter the expression and/or activity of one or more tumor suppressor proteins. In particular, the invention discloses peptides which increase the expression of p53 and/or the oncogenic mutants of p53 in vivo.

IT **625383-15-5DP**, N-terminal fluoresceinated
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptides for modulating tumor suppressor protein expression and/or activity)

IT **625383-15-5**
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptides for modulating tumor suppressor protein expression and/or activity)

L2 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 07 Nov 2003
ACCESSION NUMBER: 2003:875393 CAPLUS
DOCUMENT NUMBER: 139:363045
TITLE: Genes expressed in atherosclerotic tissue and their use in diagnosis and pharmacogenetics
INVENTOR(S): Nevins, Joseph; West, Mike; Goldschmidt, Pascal
PATENT ASSIGNEE(S): Duke University, USA
SOURCE: PCT Int. Appl., 408 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003091391	A2	20031106	WO 2002-US38221	20021112

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,

DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2003091391 A2 20031106 WO 2002-XA38221 20021112
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2003091391 A2 20031106 WO 2002-XB38221 20021112
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003224383 A1 20031204 US 2002-291885 20021112
PRIORITY APPLN. INFO.: US 2002-374547P P 20020423
US 2002-420784P P 20021024
US 2002-421043P P 20021025
US 2002-424680P P 20021108
WO 2002-US38221 A 20021112

AB Genes whose expression is correlated with an determinant of an atherosclerotic phenotype are provided. Also provided are methods of using the subject atherosclerotic determinant genes in diagnosis and treatment methods, as well as drug screening methods. In addition, reagents and kits thereof that find use in practicing the subject methods are provided. Also provided are methods of determining whether a gene is correlated with a disease phenotype, where correlation is determined using a Bayesian anal.

IT **178967-19-6**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; genes expressed in atherosclerotic tissue and their use in diagnosis and pharmacogenetics)

L2 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 29 May 2003
ACCESSION NUMBER: 2003:409169 CAPLUS
DOCUMENT NUMBER: 138:380506
TITLE: Genes that are differentially expressed during

erythropoiesis and their diagnostic and therapeutic uses

INVENTOR(S): Brissette, William H.; Neote, Kuldeep S.; Zagouras, Panayiotis; Zenke, Martin; Lemke, Britt; Hacker, Christine

PATENT ASSIGNEE(S): Pfizer Products Inc., USA; Max-Delbrueck-Centrum Fuer Molekulare Medizin

SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003038130	A2	20030508	WO 2002-XA34888	20021031
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2003038130	A2	20030508	WO 2002-US34888	20021031
WO 2003038130	A3	20040212		
WO 2003038130	C1	20040422		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:		
US 2001-335048P	P	20011031
US 2001-335183P	P	20011102
WO 2002-US34888	A	20021031

AB The present invention provides mol. targets that regulate erythropoiesis. Groups of genes or their encoded gene products comprise panels of the invention and may be used in therapeutic intervention, therapeutic agent screening, and in diagnostic methods for diseases and/or disorders of erythropoiesis. The panels were discovered using gene expression profiling of erythroid progenitors with Affymetrix HU6800 and HG-U95Av2 chips. Cells from an in vitro growth and differentiation system of SCF-Epo dependent human erythroid progenitors, E-cadherin+/CD36+ progenitors, cord blood, or CD34+ peripheral blood stem cells were analyzed. The HU6800 chip contains probes from 13,000 genes with a potential role in cell growth, proliferation, and differentiation and the HG-U95Av2 chip contains 12,000 full-length, functionally-characterized

genes. [This abstract record is one of two records for this document necessitated by the large number of index entries required to fully index the
document and publication system constraints.].

IT **178967-19-6**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; genes that are differentially expressed during erythropoiesis and their diagnostic and therapeutic uses)

L2 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 18 Apr 2003
ACCESSION NUMBER: 2003:301181 CAPLUS
DOCUMENT NUMBER: 138:316493
TITLE: Novel human proteins and cDNAs and their use in drug screening and disease diagnosis and treatment
INVENTOR(S): Alsobrook, John P., II; Burgess, Catherine E.; Catterton, Elina; Chant, John S.; Chaudhuri, Amitabha; Edinger, Shlomit R.; Gerlach, Valerie L.; Giot, Loic; Gorman, Linda; Guo, Xiaojia; Kekuda, Ramesh; Mezes, Peter S.; Millet, Isabelle; Ooi, Chean Eng; Patturajan, Meera; Rieger, Daniel K.; Spytek, Kimberly A.; Taupier, Raymond J., Jr.; Zerhusen, Bryan D.; Zhong, Haihong; Zhong, Mei
PATENT ASSIGNEE(S): Curagen Corporation, USA
SOURCE: PCT Int. Appl., 253 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 148
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003031571	A2	20030417	WO 2002-US31357		20021002
WO 2003031571	A3	20030731			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004014058	A1	20040122	US 2002-262445		20021001
US 2004038877	A1	20040226	US 2002-262839		20021001
PRIORITY APPLN. INFO.:			US 2001-327454P	P	20011005
			US 2001-327917P	P	20011009
			US 2001-328029P	P	20011009
			US 2001-328056P	P	20011009
			US 2001-328849P	P	20011012
			US 2001-329414P	P	20011015
			US 2001-330142P	P	20011017
			US 2001-341058P	P	20011022

US 2001-343629P	P	20011024
US 2001-349575P	P	20011029
US 2001-346357P	P	20011101
US 2002-391342P	P	20020625
US 2002-262445	A2	20021001
US 2001-326483P	P	20011002
US 2001-327342P	P	20011005
US 2001-328044P	P	20011009
US 2001-339266P	P	20011024
US 2002-371972P	P	20020412
US 2002-371980P	P	20020412
US 2002-373261P	P	20020417
US 2002-373805P	P	20020419
US 2002-374738P	P	20020423
US 2002-381101P	P	20020516
US 2002-381635P	P	20020517
US 2002-383830P	P	20020529

AB Disclosed herein are nucleic acid sequences that encode novel polypeptides. Also disclosed are polypeptides encoded by these nucleic acid sequences, and antibodies that immunospecifically bind to the polypeptide, as well as derivs., variants, mutants, or fragments of the novel polypeptide, polynucleotide, or antibody specific to the polypeptide. Vectors, host cells, antibodies and recombinant methods for producing the polypeptides and polynucleotides, as well as methods for using same are also included. The invention further discloses therapeutic, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins. Thus, 33 novel human cDNAs and the encoded proteins are disclosed. These display sequence homol. to various proteins, e.g., hepatocellular carcinoma-associated antigen, ferritin light chain, tumor suppressor p53-binding protein 2, etc. The expression of the genes for these proteins in various normal and diseased tissues were examined SNPs in these nucleic acids were identified. Proteins binding to TRAF and to DAPK3 were also identified.

IT **514228-34-3**, Protein NOV20a (human) **514228-35-4**, Protein NOV20b (human) **514228-36-5**, Protein NOV20c (human)
RL: ANT (Analyte); ARG (Analytical reagent use); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(amino acid sequence; novel human proteins and cDNAs and their use in drug screening and disease diagnosis and treatment)

L2 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 21 Feb 2003

ACCESSION NUMBER:	2003:133296 CAPLUS
DOCUMENT NUMBER:	138:166255
TITLE:	Stabilization of the native conformation of a mutant tumor suppressor protein p53 and other mutant proteins using CDB3 peptide and other biomolecules and application to treatment of cancer and other diseases
INVENTOR(S):	Friedler, Assaf; Fersht, Alan
PATENT ASSIGNEE(S):	Medical Research Council, UK
SOURCE:	PCT Int. Appl., 73 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003014144	A2	20030220	WO 2002-GB3668		20020809
WO 2003014144	A3	20031127			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
EP 1414846	A2	20040506	EP 2002-749128		20020809
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
US 2005008653	A1	20050113	US 2004-775679		20040210
PRIORITY APPLN. INFO.:			GB 2001-19557	A	20010810
			GB 2001-27917	A	20011121
			GB 2002-10740	A	20020510
			WO 2002-GB3668	W	20020809

AB We disclose a method of stabilizing the native state of a polypeptide, the method comprising exposing the polypeptide to a stabilizing mol. capable of binding to the polypeptide at a site which at least partially overlaps a functional site in its native state. The authors describe the isolation and identification of a stabilizing peptide CDB3, which is capable of binding the tumor suppressor protein p53 near its DNA binding site, and stabilizing the native form of the protein. Since the binding of DNA itself stabilizes p53 core domain, and it binds very tightly, stabilization by a peptide such as CDB3 is needed only for mutants where DNA binding is impaired because mutant p53 is in denatured conformation. Once the protein has bound DNA, the peptide is not needed any more. The ability of CDB3 to induce refolding of p53 core domain, together with the observation that DNA can displace it from p53, led the authors to propose the a "chaperone" mechanism for rescuing a denatured oncogenic protein: CDB3 binds only the native state of the oncogenic protein which is able to bind DNA, probably immediately on biosynthesis, and therefore shifts the equilibrium towards the native state. Then DNA can bind the protein, displacing the peptide, which is free again to bind another protein mol. Exemplary design of potential P53 core domain binding peptides, screening of the CDB peptides for binding p53 core domain, identification of the P53 core domain binding peptide CDB3, characterization of CDB3-P53 core domain binding and binding of fluorescein-labeled CDB3 are reported. Stabilizing mols. and/or compns. of the invention can be used in the treatment of any animal or human disease where errors in protein conformation, folding and aggregation contribute to the disease. Examples include cancer, cystic fibrosis and neuro-degeneration. In a particularly preferred embodiment, the disease is cancer.

IT **497259-83-3P**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(CDB3; stabilization of native conformation of human mutant tumor suppressor protein p53 and other mutant proteins using CDB3 peptide and other biomols. and application to treatment of cancer and other diseases)

IT **497259-83-3DP**, fluorescein labeled
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(stabilization of native conformation of human mutant tumor suppressor protein p53 and other mutant proteins using CDB3 peptide and other biomols. and application to treatment of cancer and other diseases)

L2 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 07 Feb 2003
ACCESSION NUMBER: 2003:97550 CAPLUS
DOCUMENT NUMBER: 138:164674
TITLE: Molecular markers for hepatocellular carcinoma and their use in diagnosis and therapy
INVENTOR(S): Debuschewitz, Sabine; Jobst, Juergen; Kaiser, Stephan
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003010336	A2	20030206	WO 2002-EP8305	20020725
WO 2003010336	A3	20041229		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10136273	A1	20030213	DE 2001-10136273	20010725
EP 1507871	A2	20050223	EP 2002-790191	20020725
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
WO 2004011945	A2	20040205	WO 2003-EP8243	20030725
WO 2004011945	A3	20040603		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,				

FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DE 2001-10136273 A 20010725
WO 2002-EP8305 W 20020725

AB The invention relates to mol. markers occurring for hepatocellular carcinoma. The invention more particularly comprises gene sequences or peptides coded thereby which can be regulated upwards or downwards for hepatic cell carcinoma (HCC) in relation to healthy, normal liver cells in the expression thereof. The invention also relates to the use of said sequences in the diagnosis and/or therapy of HCC and for screening purposes in order to identify novel active ingredients for HCC. The invention also relates to an HCC specific cluster as a unique diagnostic agent for HCC.

IT **178967-19-6**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; mol. markers for hepatocellular carcinoma)

L2 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 29 Dec 2002
ACCESSION NUMBER: 2002:978557 CAPLUS
DOCUMENT NUMBER: 138:49915
TITLE: Novel p53BP2 compounds for therapy and diagnosis and methods for using same
INVENTOR(S): Nicolette, Charles A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 39 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002197243	A1	20021226	US 2002-114091	20020401
WO 2003075831	A2	20030918	WO 2002-US10133	20020401
WO 2003075831	A3	20040617		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-280794P P 20010330

AB The present invention provides methods and compns. for detecting, diagnosing, prognosis and monitoring the progress of p53BP2-related cancers and malignancies and kits for use in said methods. Further provided are methods for screening to identify agonists and antagonists of cancer antigens associated with p53BP2-related cancers and malignancies. A composition comprising a polynucleotide encoding at least one immunogenic ligand and a host cell comprising the polynucleotide are claimed. The

composition further comprises a pharmaceutically acceptable carrier. The host
cell is a dendritic cell.

IT **479014-21-6P**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(amino acid sequence, immunogenic compound; novel p53BP2 compds. for cancer therapy and diagnosis and methods for using same)

L2 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 11 Oct 2002
ACCESSION NUMBER: 2002:777632 CAPLUS
DOCUMENT NUMBER: 137:293524
TITLE: Chimeric protein comprising immunoglobulin consensus framework and CDR sequence from p53-binding protein p53BP2 for eliciting an anti-tumor response
INVENTOR(S): Nicolette, Charles A.; Soltis, Daniel A.
PATENT ASSIGNEE(S): Purdue Pharma L.P., USA
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002078609	A2	20021010	WO 2002-US10224	20020401

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-280733P P 20010330

AB The present invention provides Igs specific for p53BP2 ligand polypeptides. In a preferred embodiment, the present invention provides a variant of an Ig variable domain, wherein the Ig variable domain contains (A) at least one CDR region and (B) framework regions flanking the CDR, and the variant includes: (a) the CDR region having added or substituted therein at least one binding sequence, and (b) the flaking framework regions, wherein the binding sequence is heterologous to the CDR and the binding sequence is derived from a human ligand having immunogenic properties relevant to human lung cancer. In a preferred embodiment, the binding sequence is an antigenic sequence. In a further preferred embodiment, the variant contains a variable domain lacking an intrachain disulfide bond.

IT **469356-94-3**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; chimeric protein comprising Ig CDRs and human lung tumor antigen p53BP2 for eliciting an anti-tumor response)

L2 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 16 Nov 2001
ACCESSION NUMBER: 2001:832384 CAPLUS
DOCUMENT NUMBER: 136:116397
TITLE: ASPP proteins specifically stimulate the apoptotic function of p53
AUTHOR(S): Samuels-Lev, Yardena; O'Connor, Daniel J.; Bergamaschi, Daniele; Trigiante, Giuseppe; Hsieh, Jung-Kuang; Zhong, Shan; Campargue, Isabelle; Naumovski, Louie; Crook, Tim; Lu, Xin
CORPORATE SOURCE: Ludwig Institute for Cancer Research, Imperial College School of Medicine, London, W2 1PG, UK
SOURCE: Molecular Cell (2001), 8(4), 781-794
CODEN: MOCEFL; ISSN: 1097-2765
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors identified a family of proteins termed ASPP. ASPP1 is a protein homologous to 53BP2, the C-terminal half of ASPP2. ASPP proteins interact with p53 and specifically enhance p53-induced apoptosis but not cell cycle arrest. Inhibition of endogenous ASPP function suppresses the apoptotic function of endogenous p53 in response to apoptotic stimuli. ASPP enhance the DNA binding and transactivation function of p53 on the promoters of proapoptotic genes in vivo. Two tumor-derived p53 mutants with reduced apoptotic function were defective in cooperating with ASPP in apoptosis induction. The expression of ASPP is frequently down-regulated in human breast carcinomas expressing wild-type p53 but not mutant p53. Therefore, ASPP regulate the tumor suppression function of p53 in vivo.
IT **389661-99-8**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; cDNA sequences of ASPP proteins that specifically stimulate apoptotic function of p53 and fail to cooperate with tumor-derived p53 mutants)
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 24 Aug 2001
ACCESSION NUMBER: 2001:618209 CAPLUS
DOCUMENT NUMBER: 135:193985
TITLE: Genes expressed in tumor cells and their use as diagnostic markers and the assessment of tumors to chemotherapy
INVENTOR(S): Roth, Frederick P.; Van Huffel, Christophe; White, James V.; Shyjan, Andrew W.
PATENT ASSIGNEE(S): Millennium Predictive Medicine, Inc., USA
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001061050	A2	20010823	WO 2001-US5301	20010216
WO 2001061050	A3	20030227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002120004	A1	20020829	US 2001-788099	20010216
US 2003129629	A1	20030710	US 2002-272111	20021016
PRIORITY APPLN. INFO.:			US 2000-183265P	P 20000217
			US 2001-788099	A1 20010216

AB The present invention is directed to the identification of markers that can be used to determine the sensitivity of cancer cells to a therapeutic agent. The present invention is also directed to the identification of therapeutic targets. Nucleic acid arrays were used to determine the level of expression of sequences (genes) found in 60 different solid tumor cancer cell lines selected from the NCI 60 cancer cell line series. Expression anal. was used to identify markers associated with sensitivity to certain chemotherapeutic agents.

IT **355485-67-5**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; genes expressed in tumor cells and their use as diagnostic markers and assessment of tumors to chemotherapy)

L2 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 24 Aug 2001
ACCESSION NUMBER: 2001:618207 CAPLUS
DOCUMENT NUMBER: 135:190398
TITLE: Nucleic acid markers useful for the identification, assessment, prevention and therapy of human cancers
INVENTOR(S): Roth, Frederick P.; Van Huffel, Christophe; White, James V.; Shyjan, Andrew W.
PATENT ASSIGNEE(S): Millennium Predictive Medicine, Inc., USA
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001061048	A2	20010823	WO 2001-US5263	20010216
WO 2001061048	A3	20030123		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,

ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002051978 A1 20020502 US 2001-788100 20010216
PRIORITY APPLN. INFO.: US 2000-183312P P 20000217

AB The present invention is directed to the identification of markers that can be used to determine the sensitivity of cancer cells to a therapeutic agent. The present invention is also directed to the identification of therapeutic targets. Nucleic acid arrays were used to determine the level of expression of sequences (genes) found in 60 different solid tumor cancer cell lines selected form the NCI 60 cancer cell line series. Expression anal. was used to identify markers associated with sensitivity to certain chemotherapeutic agents.

IT **355485-67-5**
RL: ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(amino acid sequence; nucleic acid markers useful for the identification, assessment, prevention and therapy of human cancers)

L2 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 02 Jul 1996
ACCESSION NUMBER: 1996:381500 CAPLUS
DOCUMENT NUMBER: 125:106785
TITLE: The p53-binding protein 53BP2 also interacts with Bcl2 and impedes cell cycle progression at G2/M
AUTHOR(S): Naumovski, Louie; Cleary, Michael L.
CORPORATE SOURCE: Dep. Pediatrics, Div. Hematology/Oncology, Stanford, CA, 94305, USA
SOURCE: Molecular and Cellular Biology (1996), 16(7), 3884-3892
CODEN: MCEBD4; ISSN: 0270-7306
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using the yeast two-hybrid system, we have isolated a cDNA (designated BBP, for Bcl2-binding protein) for a protein (Bbp) that interacts with Bcl2. Bbp is identical to 53BP2, a partial clone of which was previously isolated in a two-hybrid screen for proteins that interact with p53. In this study, we show that specific interactions of Bbp/53BP2 with either Bcl2 or p53 require its ankyrin repeats and SH3 domain. These interactions can be reproduced in vitro with bacterially expressed fusion proteins, and competition expts. indicate that Bcl2 prevents p53 from binding to Bbp/53BP2. BBP/53BP2 mRNA is abundant in most cell lines examined, but the protein cannot be stably expressed in a variety of cell types by transfection. In transiently transfected cells, Bbp partially colocalizes with Bcl2 in the cytoplasm and results in an increased number of cells at G2/M, possibly accounting for the inability to obtain stable transfectants expressing the protein. These results demonstrate that a single protein can interact with either Bcl2 or p53 both in yeast cells and in vitro. The in vivo significance of these interactions and their potential consequences for cell cycle progression and cell death remain to be determined

IT **178967-19-6**, Protein (human Bcl2 p53 binding reduced)

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; p53-binding protein 53BP2 also interacts with Bcl2 and impedes cell cycle progression at G2/M)

E1 THROUGH E15 ASSIGNED

FILE 'REGISTRY' ENTERED AT 15:04:12 ON 03 MAR 2005
L3 15 SEA FILE=REGISTRY ABB=ON PLU=ON (178967-19-6/BI OR 497259-83-3/BI OR 355485-67-5/BI OR 625383-15-5/BI OR 389661-99-8/BI OR 469356-94-3/BI OR 479014-21-6/BI OR 514228-34-3/BI OR 514228-35-4/BI OR 514228-36-5/BI OR 606804-01-7/BI OR 679518-01-5/BI OR 679846-54-9/BI OR 753036-25-8/BI OR 795109-26-1/BI)

L4 15 L1 AND L3

L4 ANSWER 1 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN
RN **795109-26-1** REGISTRY
CN Protein (human tumor suppressor gene ASPP2 (apoptosis stimulating proteins of p53 2)) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4: PN: US20040228866 SEQID: 4 claimed protein
CI MAN
SQL 1128

SEQ
1 MMPMFLTVYL SNNEQHFTEV PVTPETICRD VVDLCKEPGE SDCHLAEVWC
51 GSERPVADNE RMFDVLQRFG SQRNEVRFFL RHERPPGRDI VSGPRSQDPS
101 LKRNGVKVPG EYRRKENGVN SPRMDLTLAE LQEMASRQQQ QIEAQQQLLA
151 TKEQRLKFLK QQDQRQQQQV AEQEKLKRLK EIAENQEAKL KKVRALKGHV
201 EQKRLSNGKL VEEIEQMNNL FQQKQRELVL AVSKVEELTR QLEMLKNGRI
251 DSHHDNQSAV AELDRLYKEL QLRNKLNQEQ NAKLQQQREC LNKRNSEVAV
301 MDKRVNELRD RLWKKKAALQ QKENLPVSSD GNLPQQAASA PSRVAAVGPY
351 IQSSTMPRMP SRPELLVKPA LPDGSLVIQA SEGPMKIQTL PNMRSGAASQ
401 TKGSKIHPVG PDWSPSNADL FPSQGSASVP QSTGNALDQV DDGEVPLREK
451 EKKVRPFSMF DAVDQSNAPP SFGTLRKNQS SEDILRDAQV ANKNVAKVPP
501 PVPTKPKQIN LPYFGQTNQP PSDIKPDGSS QQLSTVVPSM GTKPKPAGQQ
551 PRVLLSPSIP SVGQDQTLSP GSKQESPPAA AVRPFTPQPS KDTLLPPFRK
601 PQTVAASSIY SMYTQQQAPG KNFQQAVQSA LTKTHTRGPH FSSVYGKPVI
651 AAAQNQQQHP ENIYSNSQGK PGSPEPETEP VSSVQENHEN ERIPRPLSPT
701 KLLPFLSNPY RNQSDADLEA LRKKLSNAPR PLKKRSSITE PEGPNGPNIQ
751 KLLYQRTTIA AMETISVPSY PSKSASVTAS SESPVEIQNP YLHVEPEKEV
801 VSLVPESLSP EDVGNASTEN SDMPAPSPGL DYEPEGVPDN SPNLQNNPEE
851 PNPEAPHVLD VYLEEYPPYP PPPYPSGEPE GPGEDSVSMR PPEITGQVSL
901 PPGKRTNLRK TGSERIAHGM RVKFNPLALL LDSSLEGEFD LVQRIIYEVD
951 DPSLPNDEGI TALHNAVCAG HTEIVKFLVQ FGVNVNAADS DGWTPLHCAA
1001 SCNNVQVCKF LVESGAAVFA MTYSDMQTAA DKCEEMEEGY TQCSQFLYGV
1051 QEKMGIMNKG VIYALWDYEP QNDDELPMKE GDCMTIIHRE DEDEIEWWWA
== =======
1101 RLNDKEGYVP RNLLGLYPRI KPRQRSLA

HITS AT: 1089-1097

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 141:421046

L4 ANSWER 2 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN

RN **753036-25-8** REGISTRY
CN Tumor-associated protein (human clone WO2004076614-SEQID-178 fragment) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 297: PN: WO2004076614 SEQID: 178 claimed protein
CI MAN
SQL 1101

SEQ
1 SACLGLPKCW ITGVSHHDQP LVFKKERPVA DNERMFDVLQ RFGSQRNEVR
51 FFLRHERPPG RDIVSGPRSQ DPSLKRNGVK VPGEYRRKEN GVNSPRMDLT
101 LAELQEMASR QQQQIEAQQQ LLATKEQRLK FLKQQDQRQQ QQVAEQEKLK
151 RLKEIAENQE AKLKKVRALK GHVEQKRLSN GKLVEEIEQM NNLFQQKQRE
201 LVLAVSKVEE LTRQLEMLKN GRIDSHHDNQ SAVAELDRLY KELQLRNKLN
251 QEQNAKLQQQ RECLNKRNSE VAVMDKRVNE LRDRLWKKKA ALQQKENLPV
301 SSDGNLPQQA ASAPSRVAAV GPYIQSSTMP RMPSRPELLV KPALPDGSLV
351 IQASEGPMKI QTLPNMRSGA ASQTKGSKIH PVGPDWSPSN ADLFPSQGSA
401 SVPQSTGNAL DQVDDGEVPL REKEKKVRPF SMFDAVDQSN APPSFGTLRK
451 NQSSEDILRD AQVANKNVAK VPPPVPTKPK QINLPYFGQT NQPPSDIKPD
501 GSSQQLSTVV PSMGTKPKPA GQQPRVLLSP SIPSVGQDQT LSPGSKQESP
551 PAAAVRPFTP QPSKDTLLPP FRKPQTVAAS SIYSMYTQQQ APGKNFQQAV
601 QSALTKTHTR GPHFSSVYGK PVIAAAQNQQ QHPENIYSNS QGKPGSPEPE
651 TEPVSSVQEN HENERIPRPL SPTKLLPFLS NPYRNQSDAD LEALRKKLSN
701 APRPLKKRSS ITEPEGPNGP NIQKLLYQRT TIAAMETISV PSYPSKSASV
751 TASSESPVEI QNPYLHVEPE KEVVSLVPES LSPEDVGNAS TENSDMPAPS
801 PGLDYEPEGV PDNSPNLQNN PEEPNPEAPH VLDVYLEEYP PYPPPPYPSG
851 EPEGPGEDSV SMRPPEITGQ VSLPPGKRTN LRKTGSERIA HGMRVKFNPL
901 ALLLDSSLEG EFDLVQRIIY EVDDPSLPND EGITALHNAV CAGHTEIVKF
951 LVQFGVNVNA ADSDGWTPLH CAASCNNVQV CKFLVESGAA VFAMTYSDMQ
1001 TAADKCEEME EGYTQCSQFL YGVQEKMGIM NKGVIYALWD YEPQNDDELP
1051 MKEGDCMTII HREDEDEIEW WWARLNDKEG YVPRNLLGLY PRIKPRQRSL
=========
1101 A

HITS AT: 1062-1070

REFERENCE 1: 141:258758

L4 ANSWER 3 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN
RN **679846-54-9** REGISTRY
CN Protein (mouse gene ASPP2) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 11: PN: WO2004031776 FIGURE: 4 claimed sequence
CI MAN
SQL 1128

SEQ
1 MMPMFLTVYL SNNEQHFTEV PVTPETICRD VVDLCKEPGE SDCHLAEVWC
51 GSERPVADNE RMFDVLQRFG SQRNEVRFFL RHERPPGRDI VSGPRSQDPS
101 LKRNGVKVPG EYRRKENGVN SPRMDLTLAE LQEMASRQQQ QIEAQQQLLA
151 TKEQRLKFLK QQDQRQQQQV AEQEKLKRLK EIAENQEAKL KKVRALKGHV
201 EQKRLSNGKL VEEIEQMNNL FQQKQRELVL AVSKVEELTR QLEMLKNGRI
251 DSHHDNQSAV AELDRLYKEL QLRNKLNQEQ NAKLQQQREC LNKRNSEVAV
301 MDKRVNELRD RLWKKKAALQ QKENLPVSSD GNLPQQAASA PSRVAAVGPY
351 IQSSTMPRMP SRPELLVKPA LPDGSLVIQA SEGPMKIQTL PNMRSGAASQ
401 TKGSKIHPVG PDWSPSNADL FPSQGSASVP QSTGNALDQV DDGEVPLREK
451 EKKVRPFSMF DAVDQSNAPP SFGTLRKNQS SEDILRDAQV ANKNVAKVPP
501 PVPTKPKQIN LPYFGQTNQP PSDIKPDGSS QQLSTVVPSM GTKPKPAGQQ
551 PRVLLSPSIP SVGQDQTLSP GSKQESPPAA AVRPFTPQPS KDTLLPPFRK

```
       601 PQTVAASSIY SMYTQQQAPG KNFQQAVQSA LTKTHTRGPH FSSVYGKPVI
       651 AAAQNQQQHP ENIYSNSQGK PGSPEPETEP VSSVQENHEN ERIPRPLSPT
       701 KLLPFLSNPY RNQSDADLEA LRKKLSNAPR PLKKRSSITE PEGPNGPNIQ
       751 KLLYQRTTIA AMETISVPSY PSKSASVTAS SESPVEIQNP YLHVEPEKEV
       801 VSLVPESLSP EDVGNASTEN SDMPAPSPGL DYEPEGVPDN SPNLQNNPEE
       851 PNPEAPHVLD VYLEEYPPYP PPPYPSGEPE GPGEDSVSMR PPEITGQVSL
       901 PPGKRTNLRK TGSERIAHGM RVKFNPLALL LDSSLEGEFD LVQRIIYEVD
       951 DPSLPNDEGI TALHNAVCAG HTEIVKFLVQ FGVNVNAADS DGWTPLHCAA
      1001 SCNNVQVCKF LVESGAAVFA MTYSDMQTAA DKCEEMEEGY TQCSQFLYGV
      1051 QEKMGIMNKG VIYALWDYEP QNDDELPMKE GDCMTIIHRE DEDEIEWWWA
                                                    == =======
      1101 RLNDKEGYVP RNLLGLYPRI KPRQRSLA
HITS AT:   1089-1097

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE   1:  140:333564

L4   ANSWER 4 OF 15  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   679518-01-5  REGISTRY
CN   7: PN: WO2004031229 FIGURE: 10 unclaimed sequence (9CI)  (CA INDEX NAME)
CI   MAN
SQL  179

SEQ      1 DDPSLPNDEG ITALHNAVCA GHTEIVKFLV QFGVNVNAAD SDGWTPLHCA
         51 ASCNNVQVCK FLVESGAAVF AMTYSDMQTA ADKCEEMEEG YTQCSQFLYG
        101 VQEKMGIMNK GVIYALWDYE PQNDDELPMK EGDCMTIIHR EDEDEIEWWW
                                                    = ========
        151 ARLNDKEGYV PRNLLGLYPR IKPRQRSLA
HITS AT:   140-148

REFERENCE   1:  140:332473

L4   ANSWER 5 OF 15  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   625383-15-5  REGISTRY
CN   L-Tryptophanamide, L-arginyl-L-α-glutamyl-L-α-aspartyl-L-
     α-glutamyl-L-α-aspartyl-L-α-glutamyl-L-isoleucyl-L-
     α-glutamyl- (9CI)  (CA INDEX NAME)
SQL  9

SEQ      1 REDEDEIEW
           =========
HITS AT:   1-9

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE   1:  139:391336

L4   ANSWER 6 OF 15  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   606804-01-7  REGISTRY
CN   TP53BP2 protein (human clone MGC:65089 IMAGE:4537206) (9CI)  (CA INDEX
     NAME)
OTHER NAMES:
CN   GenBank AAH58918
CN   GenBank AAH58918 (Translated from: GenBank BC058918)
CI   MAN
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SQL 1127

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SEQ      1 MPMFLTVYLS NNEQHFTEVP VTPETICRDV VDLCKEPGES DCHLAEVWCG
        51 SERPVADNER MFDVLQRFGS QRNEVRFFLR HERPPGRDIV SGPRSQDPSL
       101 KRNGVKVPGE YRRKENGVNS PRMDLTLAEL QEMASRQQQQ IEAQQQLLAT
       151 KEQRLKFLKQ QDQRQQQQVA EQEKLKRLKE IAENQEAKLK KVRALKGHVE
       201 QKRLSNGKLV EEIEQMNNLF QQKQRELVLA VSKVEELTRQ LEMLKNGRID
       251 SHHDNQSAVA ELDRLYKELQ LRNKLNQEQN AKLQQQRECL NKRNSEVAVM
       301 DKRVNELRDR LWKKKAALQQ KENLPVSSDG NLPQQAASAP SRVAAVGPYI
       351 QSSTMPRMPS RPELLVKPAL PDGSLVIQAS EGPMKIQTLP NMRSGAASQT
       401 KGSKIHPVGP DWSPSNADLF PSQGSASVPQ STGNALDQVD DGEVPLREKE
       451 KKVRPFSMFD AVDQSNAPPS FGTLRKNQSS EDILRDAQVA NKNVAKVPPP
       501 VPTKPKQINL PYFGQTNQPP SDIKPDGSSQ QLSTVVPSMG TKPKPAGQQP
       551 RVLLSPSIPS VGQDQTLSPG SKQESPPAAA VRPFTPQPSK DTLLPPFRKP
       601 QTVAASSIYS MYTQQQAPGK NFQQAVQSAL TKTHTRGPHF SSVYGKPVIA
       651 AAQNQQQHPE NIYSNSQGKP GSPEPETEPV SSVQENHENE RIPRPLSPTK
       701 LLPFLSNPYR NQSDADLEAL RKKLSNAPRP LKKRSSITEP EGPNGPNIQK
       751 LLYQRTTIAA METISVPSYP SKSASVTASS ESPVEIQNPY LHVEPEKEVV
       801 SLVPESLSPE DVGNASTENS DMPAPSPGLD YEPEGVPDNS PNLQNNPEEP
       851 NPEAPHVLDV YLEEYPPYPP PPYPSGEPEG PGEDSVSMRP PEITGQVSLP
       901 PGKRTNLRKT GSERIAHGMR VKFNPLALLL DSSLEGEFDL VQRIIYEVDD
       951 PSLPNDEGIT ALHNAVCAGH TEIVKFLVQF GVNVNAADSD GWTPLHCAAS
      1001 CNNVQVCKFL VESGAAVFAM TYSDMQTAAD KCEEMEEGYT QCSQFLYGVQ
      1051 EKMGIMNKGV IYALWDYEPQ NDDELPMKEG DCMTIIHRED EDEIEWWWAR
                                                    === ======
      1101 LNDKEGYVPR NLLGLYPRIK PRQRSLA
HITS AT:   1088-1096
```

REFERENCE 1: 142:18208

L4 ANSWER 7 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN
RN **514228-36-5** REGISTRY
CN Protein NOV20c (human) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 65: PN: WO03031571 SEQID: 66 claimed protein
CI MAN
SQL 1001

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SEQ      1 MFDVLQRFGS QRNEVRFFLR HERPPGRDIV SGPRSQDPSL KRNGVKVPGE
        51 YRRKENGVNS PRMDLTLAEL QEMASRQQQQ IEAQQQLLAT KEQRLKFLKQ
       101 QDQRQQQQVA EQEKLKRLKE IAENQEAKLK KVRALKGHVE QKRLSNGKLV
       151 EEIEQMNNLF QQKQRELVLA VSKVEELTRQ LEMLKNGRID SHHDNQSAVA
       201 ELDRLYKELQ LRNKLNQEQN AKLQQQRECL NKRNSEVAVM DKRVNELRDR
       251 LWKKKAALQQ KENLPVSSDG NLPQQAASAP SRVAAVGPYI QSSTMPRMPS
       301 RPELLVKPAL PDGSLVIQAS EGPMKIQTLP NMRSGAASQT KGSKIHPVGP
       351 DWSPSNADLF PSQGSASVPQ STGNALDQVD DGEVPLREKE KKVRPFSMFD
       401 AVDQSNAPPS FGTLRKNQSS EDILRDAQVA NKNVAKVPPP VPTKPKQINL
       451 PYFGQTNQPP SDIKPDGSSQ QLSTVVPSMG TKPKPAGQQP RVLLSPSIPS
       501 VGQDQTLSPG SKQESPPAAA VRPFTPQPSK DTLLPPFRKP QTVAASSIYS
       551 MYTQQQAPGK NFQQAVQSAL TKTHTRGPHF SSVYGKPVIA AAQNQQQHPE
       601 NIYSNSQGKP GSPEPETEPV SSVQENHENE RIPRPLSPTK LLPFLSNPYR
       651 NQSDADLEAL RKKLSNAPRP LKKRSSITEP EGPNGPNIQK LLYQRTTIAA
       701 METISVPSYP SKSASVTASS ESPVEIQNPH VLDVYLEEYP PYPPPPYPSG
       751 EPEGPGEDSV SMRPPEITGQ VSLPPGKRTN LRKTGSERIA HGMRVKFNPL
       801 ALLLDSSLEG EFDLVQRIIY EVDDPSLPND EGITALHNAV CAGHTEIVKF
       851 LVQFGVNVNA ADSDGWTPLH CAASCNNVQV CKFLVESGAA VFAMTYSDMQ
```

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       901 TAADKCEEME EGYTQCSQFL YGVQEKMGIM NKGVIYALWD YEPQNDDELP
       951 MKEGDCMTII HREDEDEIEW WWARLNDKEG YVPRNLLGLY PRIKPRQRSL
                   =========

      1001 A
HITS AT:   962-970

REFERENCE   1:  138:316493

L4   ANSWER 8 OF 15  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   514228-35-4  REGISTRY
CN   Protein NOV20b (human) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   63: PN: WO03031571 SEQID: 64 claimed protein
CI   MAN
SQL  1068

SEQ      1 MRFGSKMMPM FLTVYLSNNE QHFTEVPVTP ETICRDVVDL CKEPGESDCH
        51 LAEVWCGSER PVADNERMFD VLQRFGSQRN EVRFFLRHER PPGRDIVSGP
       101 RSQDPSLKRN GVKVPGEYRR KENGVNSPRM DLTLAELQEM ASRQQQQIEA
       151 QQQLLATKEQ RLKFLKQQDQ RQQQQVAEQE KLKRLKEIAE NQEAKLKKVR
       201 ALKGHVEQKR LSNGKLVEEI EQMNNLFQQK QRELVLAVSK VEELTRQLEM
       251 LKNGRIDSHH DNQSAVAELD RLYKELQLRN KLNQEQNAKL QQQRECLNKR
       301 NSEVAVMDKR VNELRDRLWK KKAALQQKEN LPVSSDGNLP QQAASAPSRV
       351 AAVGPYIQSS TMPRMPSRPE LLVKPALPDG SLVIQASEGP MKIQTLPNMR
       401 SGAASQTKGS KIHPVGPDWS PSNADLFPSQ GSASVPQSTG NALDQVDDGE
       451 VPLREKEKKV RPFSMFDAVD QSNAPPSFGT LRKNQSSEDI LRDAQVANKN
       501 VAKVPPPVPT KPKQINLPYF GQTNQPPSDI KPDGSSQQLS TVVPSMGTKP
       551 KPAGQQPRVL LSPSIPSVGQ DQTLSPGSKQ ESPPAAAVRP FTPQPSKDTL
       601 LPPFRKPQTV AASSIYSMYT QQQAPGKNFQ QAVQSALTKT HTRGPHFSSV
       651 YGKPVIAAAQ NQQQHPENIY SNSQGKPGSP EPETEPVSSV QENHENERIP
       701 RPLSPTKLLP FLSNPYRNQS DADLEALRKK LSNAPRPLKK RSSITEPEGP
       751 NGPNIQKLLY QRTTIAAMET ISVPSYPSKS ASVTASSESP VEIQNPHVLD
       801 VYLEEYPPYP PPPYPSGEPE GPGEDSVSMR PPEITGQVSL PPGKRTNLRK
       851 TGSERIAHGM RVKFNPLALL LDSSLEGEFD LVQRIIYEVD DPSLPNDEGI
       901 TALHNAVCAG HTEIVKFLVQ FGVNVNAADS DGWTPLHCAA SCNNVQVCKF
       951 LVESGAAVFA MTYSDMQTAA DKCEEMEEGY TQCSQFLYGV QEKMGIMNKG
      1001 VIYALWDYEP QNDDELPMKE GDCMTIIHRE DEDEIEWWWA RLNDKEGYVP
                                        == =======
      1051 RNLLGLYPRI KPRQRSLA
HITS AT:   1029-1037

REFERENCE   1:  138:316493

L4   ANSWER 9 OF 15  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   514228-34-3  REGISTRY
CN   Protein NOV20a (human) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   61: PN: WO03031571 SEQID: 62 claimed protein
CI   MAN
SQL  1005

SEQ      1 MDLTLAELQE MASRQQQQIE AQQQLLATKE QRLKFLKQQD QRQQQQVAEQ
        51 EKLKRLKEIA ENQEAKLKKV RALKGHVEQK RLSNGKLVEE IEQMNNLFQQ
       101 KQRELVLAVS KVEELTRQLE MLKNGRIDSH HDNQSAVAEL DRLYKELQLR
       151 NKLNQEQNAK LQQQRECLNK RNSEVAVMDK RVNELRDRLW KKKAALQQKE
       201 NLPVSSDGNL PQQAASAPSR VAAVGPYIQS STMPRMPSRP ELLVKPALPD
```

```
        251 GSLVIQASEG PMKIQTLPNM RSGAASQTKG SKIHPVGPDW SPSNADLFPS
        301 QGSASVPQST GNALDQVDDG EVPLREKEKK VRPFSMFDAV DQSNAPPSFG
        351 TLRKNQSSED ILRDAQVANK NVAKVPPPVP TKPKQINLPY FGQTNQPPSD
        401 IKPDGSSQQL STVVPSMGTK PKPAGQQPRV LLSPSIPSVG QDQTLSPGSK
        451 QESPPAAAVR PFTPQPSKDT LLPPFRKPQT VAASSIYSMY TQQQAPGKNF
        501 QQAVQSALTK THTRGPHFSS VYGKPVIAAA QNQQQHPENI YSNSQGKPGS
        551 PEPETEPVSS VQENHENERI PRPLSPTKLL PFLSNPYRNQ SDADLEALRK
        601 KLSNAPRPLK KRSSITEPEG PNGPNIQKLL YQRTTIAAME TISVPSYPSK
        651 SASVTASSES PVEIQNPYLH VEPEKEVVSL VPESLSPEDV GNASTENSDM
        701 PAPSPGLDYE PEGVPDNSPN LQNNPEEPNP EAPHVLDVYL EEYPPYPPPP
        751 YPSGEPEGPG EDSVSMRPPE ITGQVSLPPG KRTNLRKTGS ERIAHGMRVK
        801 FNPLALLLDS SLEGEFDLVQ RIIYEVDDPS LPNDEGITAL HNAVCAGHTE
        851 IVKFLVQFGV NVNAADSDGW TPLHCAASCN NVQVCKFLVE SGAAVFAMTY
        901 SDMQTAADKC EEMEEGYTQC SQFLYGVQEK MGIMNKGVIY ALWDYEPQND
        951 DELPMKEGDC MTIIHREDED EIEWWWARLN DKEGYVPRNL LGLYPRIKPR
                            ===== ====

       1001 QRSLA
HITS AT:    966-974

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE   1:  138:316493

L4   ANSWER 10 OF 15  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   497259-83-3  REGISTRY
CN   L-Tryptophan, L-arginyl-L-α-glutamyl-L-α-aspartyl-L-α-
     glutamyl-L-α-aspartyl-L-α-glutamyl-L-isoleucyl-L-α-
     glutamyl- (9CI)  (CA INDEX NAME)
SQL  9

SEQ       1 REDEDEIEW
            =========
HITS AT:    1-9

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE   1:  140:104698

REFERENCE   2:  138:166255

L4   ANSWER 11 OF 15  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   479014-21-6  REGISTRY
CN   Protein p53BP2 (p53-binding protein 2) (human) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   3: PN: US20020197243 SEQID: 2 claimed protein
CI   MAN
SQL  1005

SEQ       1 MDLTLAELQE MASRQQQQIE AQQQLLATKE QRLKFLKQQD QRQQQQVAEQ
         51 EKLKRLKEIA ENQEAKLKKV RALKGHVEQK RLSNGKLVEE IEQMNNLFQQ
        101 KQRELVLAVS KVEELTRQLE MLKNGRIDSH HDNQSAVAEL DRLYKELQLR
        151 NKLNQEQNAK LQQQRECLNK RNSEVAVMDK RVNELRDRLW KKKAALQQKE
        201 NLPVSSDGNL PQQAASAPSR VAAVGPYIQS STMPRMPSRP ELLVKPALPD
        251 GSLVIQASEG PMKIQTLPNM RSGAASQTKG SKIHPVGPDW SPSNADLFPS
        301 QGSASVPQST GNALDQVDDG EVPLREKEKK VRPFSMFDAV DQSNAPPSFG
        351 TLRKNQSSED ILRDAQVANK NVAKVPPPVP TKPKQINLPY FGQTNQPPSD
```

```
       401 IKPDGSSQQL STVVPSMGTK PKPAGQQPRV LLSPSIPSVG QDQTLSPGSK
       451 QESPPAAAVR PFTPQPSKDT LLPPFRKPQT VAASSIYSMY TQQQAPGKNF
       501 QQAVQSALTK THTRGPHFSS VYGKPVIAAA QNQQQHPENI YSNSQGKPGS
       551 PEPETEPVSS VQENHENERI PRPLSPTKLL PFLSNPYRNQ SDADLEALRK
       601 KLSNAPRPLK KRSSITEPEG PNGPNIQKLL YQRTTIAAME TISVPSYPSK
       651 SASVTASSES PVEIQNPYLH VEPEKEVVSL VPESLSPEDV GNASTENSDM
       701 PAPSPGLDYE PEGVPDNSPN LQNNPEEPNP EAPHVLDVYL EEYPPYPPPP
       751 YPSGEPEGPG EDSVSMRPPE ITGQVSLPPG KRTNLRKTGS ERIAHGMRVK
       801 FNPLALLLDS SLEGEFDLVQ RIIYEVDDPS LPNDEGITAL HNAVCAGHTE
       851 IVKFLVQFGV NVNAADSDGW TPLHCAASCN NVQVCKFLVE SGAAVFAMTY
       901 SDMQTAADKC EEMEEGYTQC SQFLYGVQEK MGIMNKGVIY ALWDYEPQND
       951 DELPMKEGDC MTIIHREDED EIEWWWARLN DKEGYVPRNL LGLYPRIKPR
                           ===== ====
      1001 QRSLA
HITS AT:    966-974

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE   1:  138:49915

L4   ANSWER 12 OF 15  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   469356-94-3  REGISTRY
CN   Protein p53BP2 (p53-binding protein) (human) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   2: PN: WO02078609 SEQID: 2 claimed protein
CI   MAN
SQL  1005

SEQ      1 MDLTLAELQE MASRQQQQIE AQQQLLATKE QRLKFLKQQD QRQQQQVAEQ
        51 EKLKRLKEIA ENQEAKLKKV RALKGHVEQK RLSNGKLVEE IEQMNNLFQQ
       101 KQRELVLAVS KVEELTRQLE MLKNGRIDSH HDNQSAVAEL DRLYKELQLR
       151 NKLNQEQNAK LQQQRECLNK RNSEVAVMDK RVNELRDRLW KKKAALQQKE
       201 NLPVSSDGNL PQQAASAPSR VAAVGPYIQS STMPRMPSRP ELLVKPALPD
       251 GSLVIQASEG PMKIQTLPNM RSGAASQTKG SKIHPVGPDW SPSNADLFPS
       301 QGSASVPQST GNALDQVDDG EVPLREKEKK VRPFSMFDAV DQSNAPPSFG
       351 TLRKNQSSED ILRDAQVANK NVAKVPPPVP TKPKQINLPY FGQTNQPPSD
       401 IKPDGSSQQL STVVPSMGTK PKPAGQQPRV LLSPSIPSVG QDQTLSPGSK
       451 QESPPAAAVR PFTPQPSKDT LLPPFRKPQT VAASSIYSMY TQQQAPGKNF
       501 QQAVQSALTK THTRGPHFSS VYGKPVIAAA QNQQQHPENI YSNSQGKPGS
       551 PEPETEPVSS VQENHENERI PRPLSPTKLL PFLSNPYRNQ SDADLEALRK
       601 KLSNAPRPLK KRSSITEPEG PNGPNIQKLL YQRTTIAAME TISVPSYPSK
       651 SASVTASSES PVEIQNPYLH VEPEKEVVSL VPESLSPEDV GNASTENSDM
       701 PAPSPGLDYE PEGVPDNSPN LQNNPEEPNP EAPHVLDVYL EEYPPYPPPP
       751 YPSGEPEGPG EDSVSMRPPE ITGQVSLPPG KRTNLRKTGS ERIAHGMRVK
       801 FNPLALLLDS SLEGEFDLVQ RIIYEVDDPS LPNDEGITAL HNAVCAGHTE
       851 IVKFLVQFGV NVNAADSDGW TPLHCAASCN NVQVCKFLVE SGAAVFAMTY
       901 SDMQTAADKC EEMEEGYTQC SQFLYGVQEK MGIMNKGVIY ALWDYEPQND
       951 DELPMKEGDC MTIIHREDED EIEWWWARLN DKEGYVPRNL LGLYPRIKPR
                           ===== ====
      1001 QRSLA
HITS AT:    966-974

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE   1:  137:293524
```

L4 ANSWER 13 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN
RN **389661-99-8** REGISTRY
CN transcription factor ASPP2 (apoptosis-stimulating protein of p53 2) (human gene ASPP2) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN ASPP2 protein (human gene ASPP2)
CN GenBank CAC83012
CN GenBank CAC83012 (Translated from: GenBank AJ318888)
CI MAN
SQL 1128

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SEQ      1 MMPMFLTVYL SNNEQHFTEV PVTPETICRD VVDLCKEPGE SDCHLAEVWC
        51 GSERPVADNE RMFDVLQRFG SQRNEVRFFL RHERPPGRDI VSGPRSQDPS
       101 LKRNGVKVPG EYRRKENGVN SPRMDLTLAE LQEMASRQQQ QIEAQQQLLA
       151 TKEQRLKFLK QQDQRQQQQV AEQEKLKRLK EIAENQEAKL KKVRALKGHV
       201 EQKRLSNGKL VEEIEQMNNL FQQKQRELVL AVSKVEELTR QLEMLKNGRI
       251 DSHHDNQSAV AELDRLYKEL QLRNKLNQEQ NAKLQQQREC LNKRNSEVAV
       301 MDKRVNELRD RLWKKKAALQ QKENLPVSSD GNLPQQAASA PSRVAAVGPY
       351 IQSSTMPRMP SRPELLVKPA LPDGSLVIQA SEGPMKIQTL PNMRSGAASQ
       401 TKGSKIHPVG PDWSPSNADL FPSQGSASVP QSTGNALDQV DDGEVPLREK
       451 EKKVRPFSMF DAVDQSNAPP SFGTLRKNQS SEDILRDAQV ANKNVAKVPP
       501 PVPTKPKQIN LPYFGQTNQP PSDIKPDGSS QQLSTVVPSM GTKPKPAGQQ
       551 PRVLLSPSIP SVGQDQTLSP GSKQESPPAA AVRPFTPQPS KDTLLPPFRK
       601 PQTVAASSIY SMYTQQQAPG KNFQQAVQSA LTKTHTRGPH FSSVYGKPVI
       651 AAAQNQQQHP ENIYSNSQGK PGSPEPETEP VSSVQENHEN ERIPRPLSPT
       701 KLLPFLSNPY RNQSDADLEA LRKKLSNAPR PLKKRSSITE PEGPNGPNIQ
       751 KLLYQRTTIA AMETISVPSY PSKSASVTAS SESPVEIQNP YLHVEPEKEV
       801 VSLVPESLSP EDVGNASTEN SDMPAPSPGL DYEPEGVPDN SPNLQNNPEE
       851 PNPEAPHVLD VYLEEYPPYP PPPYPSGEPE GPGEDSVSMR PPEITGQVSL
       901 PPGKRTNLRK TGSERIAHGM RVKFNPLALL LDSSLEGEFD LVQRIIYEVD
       951 DPSLPNDEGI TALHNAVCAG HTEIVKFLVQ FGVNVNAADS DGWTPLHCAA
      1001 SCNNVQVCKF LVESGAAVFA MTYSDMQTAA DKCEEMEEGY TQCSQFLYGV
      1051 QEKMGIMNKG VIYALWDYEP QNDDELPMKE GDCMTIIHRE DEDEIEWWWA
                                                    == =======
      1101 RLNDKEGYVP RNLLGLYPRI KPRQRSLA
HITS AT:   1089-1097
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RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 136:116397

L4 ANSWER 14 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN
RN **355485-67-5** REGISTRY
CN Protein (human clone 53BP2 p53-binding C-terminal fragment) (9CI) (CA INDEX NAME)
CI MAN
SQL 529

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SEQ      1 KPQTVAASSI YSMYTQQQAP GKNFQQAVQS ALTKTHTRGP HFSSVYGKPV
        51 IAAAQNQQQH PENIYSNSQG KPGSPEPETE PVSSVQENHE NERIPRPLSP
       101 TKLLPFLSNP YRNQSDADLE ALRKKLSNAP RPLKKRSSIT EPEGPNGPNI
       151 QKLLYQRTTI AAMETISVPS YPSKSASVTA SSESPVEIQN PYLHVEPEKE
       201 VVSLVPESLS PEDVGNASTE NSDMPAPSPG LDYEPEGVPD NSPNLQNNPE
       251 EPNPEAPHVL DVYLEEYPPY PPPPYPSGEP EGPGEDSVSM RPPEITGQVS
       301 LPPGKRTNLR KTGSERIAHG MRVKFNPLAL LLDSSLEGEF DLVQRIIYEV
       351 DDPSLPNDEG ITALHNAVCA GHTEIVKFLV QFGVNVNAAD SDGWTPLHCA
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401 ASCNNVQVCK FLVESGAAVF AMTYSDMQTA ADKCEEMEEG YTQCSQFLYG
451 VQEKMGIMNK GVIYALWDYE PQNDDELPMK EGDCMTIIHR EDEDEIEWWW
= ========
501 ARLNDKEGYV PRNLLGLYPR IKPRQRSLA
HITS AT: 490-498

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 135:193985

REFERENCE 2: 135:190398

L4 ANSWER 15 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN
RN **178967-19-6** REGISTRY
CN bcl-2 protein (human p53-binding reduced) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2098: PN: WO03095618 TABLE: 1 claimed protein
CN 290: PN: WO03010336 TABLE: 1B claimed protein
CN 3040: PN: WO03038130 FIGURE: 3 claimed protein
CN 3493: PN: WO03091391 FIGURE: 20 unclaimed protein
CN 569: PN: WO2004038376 TABLE: 5 unclaimed protein
CN 635: PN: WO03091391 FIGURE: 19 unclaimed protein
CN Bbp/53BP2 (human cell line HAL-01; B-cell progenitor cell line gene BBP/53BP2)
CN GenBank AAC50557
CN GenBank AAC50557 (Translated from: GenBank U58334)
CN Protein Bcl2 (human p53-binding reduced)
CI MAN
SQL 1005

SEQ 1 MDLTLAELQE MASRQQQQIE AQQQLLATKE QRLKFLKQQD QRQQQQVAEQ
51 EKLKRLKEIA ENQEAKLKKV RALKGHVEQK RLSNGKLVEE IEQMNNLFQQ
101 KQRELVLAVS KVEELTRQLE MLKNGRIDSH HDNQSAVAEL DRLYKELQLR
151 NKLNQEQNAK LQQQRECLNK RNSEVAVMDK RVNELRDRLW KKKAALQQKE
201 NLPVSSDGNL PQQAASAPSR VAAVGPYIQS STMPRMPSRP ELLVKPALPD
251 GSLVIQASEG PMKIQTLPNM RSGAASQTKG SKIHPVGPDW SPSNADLFPS
301 QGSASVPQST GNALDQVDDG EVPLREKEKK VRPFSMFDAV DQSNAPPSFG
351 TLRKNQSSED ILRDAQVANK NVAKVPPPVP TKPKQINLPY FGQTNQPPSD
401 IKPDGSSQQL STVVPSMGTK PKPAGQQPRV LLSPSIPSVG QDQTLSPGSK
451 QESPPAAAVR PFTPQPSKDT LLPPFRKPQT VAASSIYSMY TQQQAPGKNF
501 QQAVQSALTK THTRGPHFSS VYGKPVIAAA QNQQQHPENI YSNSQGKPGS
551 PEPETEPVSS VQENHENERI PRPLSPTKLL PFLSNPYRNQ SDADLEALRK
601 KLSNAPRPLK KRSSITEPEG PNGPNIQKLL YQRTTIAAME TISVPSYPSK
651 SASVTASSES PVEIQNPYLH VEPEKEVVSL VPESLSPEDV GNASTENSDM
701 PAPSPGLDYE PEGVPDNSPN LQNNPEEPNP EAPHVLDVYL EEYPPYPPPP
751 YPSGEPEGPG EDSVSMRPPE ITGQVSLPPG KRTNLRKTGS ERIAHGMRVK
801 FNPLALLLDS SLEGEFDLVQ RIIYEVDDPS LPNDEGITAL HNAVCAGHTE
851 IVKFLVQFGV NVNAADSDGW TPLHCAASCN NVQVCKFLVE SGAAVFAMTY
901 SDMQTAADKC EEMEEGYTQC SQFLYGVQEK MGIMNKGVIY ALWDYEPQND
951 DELPMKEGDC MTIIHREDED EIEWWWARLN DKEGYVPRNL LGLYPRIKPR
===== ====
1001 QRSLA
HITS AT: 966-974

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 140:420388

REFERENCE 2: 140:40262

REFERENCE 3: 139:379453

REFERENCE 4: 139:363045

REFERENCE 5: 138:380506

REFERENCE 6: 138:164674

REFERENCE 7: 125:106785

(FILE 'MEDLINE, BIOSIS, EMBASE, CANCERLIT' ENTERED AT 15:05:31 ON 03 MAR 2005)
L5 0 S L4

-key terms Claim 26

(FILE 'CAPLUS' ENTERED AT 15:05:50 ON 03 MAR 2005)
L6 86 SEA FILE=CAPLUS ABB=ON PLU=ON R175H OR G245S OR R248Q OR R249S OR R273H OR R282W OR I195T
L7 83 SEA FILE=CAPLUS ABB=ON PLU=ON L6(S)(MUTAT? OR MUTANT OR MUTAGEN? OR POLYMORPH?)
L8 71 SEA FILE=CAPLUS ABB=ON PLU=ON L7 AND P53
L9 22 SEA FILE=CAPLUS ABB=ON PLU=ON L8 AND (STABIL? OR STABLE?)

L10 21 L9 NOT L2

L10 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 25 Oct 2004
ACCESSION NUMBER: 2004:884446 CAPLUS
DOCUMENT NUMBER: 141:360334
TITLE: CP-31398 Restores DNA-binding Activity to Mutant **p53** in Vitro but Does Not Affect **p53** Homologs p63 and p73
AUTHOR(S): Demma, Mark J.; Wong, Serena; Maxwell, Eugene; Dasmahapatra, Bimalendu
CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA
SOURCE: Journal of Biological Chemistry (2004), 279(44), 45887-45896
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **p53** protein plays a major role in the maintenance of genome **stability** in mammalian cells. Mutations of **p53** occur in over 50% of all cancers and are indicative of highly aggressive cancers that are hard to treat. Recently, there has been a high degree of interest in therapeutic approaches to restore growth suppression functions to mutant **p53**. Several compds. have been reported to restore wild type function to mutant **p53**. One such compound, CP-31398, has been shown effective in vivo, but questions have arisen to whether it actually affects **p53**. Here we show that mutant **p53**,

isolated from cells treated with CP-31398, is capable of binding to **p53** response elements in vitro. We also show the compound restores DNA-binding activity to mutant **p53** in cells as determined by a chromatin immunopptn. assay. In addition, using purified **p53** core domain from two different hotspot **mutants** (**R273H** and **R249S**), we show that CP-31398 can restore DNA-binding activity in a dose-dependent manner. Using a quant. DNA binding assay, we also show that CP-31398 increases significantly the amount of mutant **p53** that binds to cognate DNA (Bmax) and its affinity (Kd) for DNA. The compound, however, does not affect the affinity (Kd value) of wild type **p53** for DNA and only increases Bmax slightly. In a similar assay PRIMA1 does not have any effect on **p53** core DNA-binding activity. We also show that CP-31398 had no effect on the DNA-binding activity of **p53** homologs p63 and p73.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 13 May 2004
ACCESSION NUMBER: 2004:386272 CAPLUS
DOCUMENT NUMBER: 141:420098
TITLE: Mutant **p53** expression enhances drug resistance in a hepatocellular carcinoma cell line
AUTHOR(S): Chan, Kin-Tak; Lung, Maria Li
CORPORATE SOURCE: Department of Biology, The Hong Kong University of Science and Technology, Hong Kong (SAR), Peop. Rep. China
SOURCE: Cancer Chemotherapy and Pharmacology (2004), 53(6), 519-526
CODEN: CCPHDZ; ISSN: 0344-5704
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Chemoresistance is a major problem in the treatment of hepatocellular carcinoma. Certain **p53** mutants may enhance drug resistance in cancer cells. To determine whether two frequently occurring **p53 mutants, R248Q** and R273C, would increase the drug resistance of liver cancer cells, **stable** cell lines expressing these specific **p53 mutants** were established by transfecting the **p53**-null Hep3B cells with **mutant p53** expression vectors, and then treating them with the anticancer drugs doxorubicin and paclitaxel. The cells expressing the **p53 mutant, R248Q**, but not R273C, displayed cross-resistance to both drugs, in contrast to the control cells expressing the vector alone. Moreover, both the expression and the activity of the multiple drug resistance gene product, P-glycoprotein, were elevated in **p53 mutant R248Q**-expressing cells. Reduced uptake of doxorubicin was also observed in the R248Q-expressing cells. These results suggest that expression of the **p53 mutant, R248Q**, in liver cancer cells may enhance their drug resistance and that upregulation of P-glycoprotein activity may contribute to this protective effect.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 25 Mar 2004
ACCESSION NUMBER: 2004:245726 CAPLUS
DOCUMENT NUMBER: 140:401217
TITLE: Mutant **p53** exerts a dominant negative effect by preventing wild-type **p53** from binding to the promoter of its target genes
AUTHOR(S): Willis, Amy; Jung, Eun Joo; Wakefield, Therese; Chen, Xinbin
CORPORATE SOURCE: Department of Cell Biology and UAB Comprehensive Cancer Center, The University of Alabama at Birmingham, Birmingham, AL, 35294-0005, USA
SOURCE: Oncogene (2004), 23(13), 2330-2338
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mutation of the **p53** tumor suppressor gene is the most common genetic alteration in human cancer. A majority of these mutations are missense mutations in the DNA-binding domain. As a result, the mutated **p53** gene encodes a full-length protein incapable of transactivating its target genes. In addition to this loss of function, mutant **p53** can have a dominant neg. effect over wild-type **p53** and/or gain of function activity independently of the wild-type protein. To better understand the nature of the tumorigenic activity of mutant **p53**, we have investigated the mechanism by which mutant **p53** can exert a dominant neg. effect. We have established several **stable** cell lines capable of inducibly expressing a **p53** mutant alone, wild-type **p53** alone, or both proteins concurrently. In this context, we have used chromatin immunopptn. to determine the ability of wild-type **p53** to bind to its endogenous target genes in the presence of various **p53** mutants. We have found that **p53** missense mutants markedly reduce the binding of wild-type **p53** to the **p53** responsive element in the target genes of p21, MDM2, and PIG3. These findings correlate with the reduced ability of wild-type **p53** in inducing these and other endogenous target genes and growth suppression in the presence of mutant **p53**. We also showed that mutant **p53** suppresses the ability of wild-type **p53** in inducing cell cycle arrest. This highlights the sensitivity and utility of the dual inducible expression system because in previous studies, **p53**-mediated cell cycle arrest is not affected by transiently overexpressed **p53** mutants. Together, our data showed that mutant **p53** exerts its dominant neg. activity by abrogating the DNA binding, and subsequently the growth suppression, functions of wild-type **p53**.
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 22 Dec 2003
ACCESSION NUMBER: 2003:992974 CAPLUS
DOCUMENT NUMBER: 140:57487
TITLE: **P53** hot-spot mutants are resistant to ubiquitin-independent degradation by increased binding to NAD(P)H:Quinone oxidoreductase 1
AUTHOR(S): Asher, Gad; Lotem, Joseph; Tsvetkov, Peter; Reiss, Veronica; Sachs, Leo; Shaul, Yosef

CORPORATE SOURCE: Department of Molecular Genetics, Weizmann Institute of Science, Rehovot, 76100, Israel
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(25), 15065-15070
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Proteasomal degradation of **p53** is mediated by two alternative pathways that are either dependent or independent of both Mdm2 and ubiquitin. The ubiquitin-independent pathway is regulated by NAD(P)H: quinone oxidoreductase 1 (NQO1) that **stabilizes p53**. The NQO1 inhibitor dicoumarol induces ubiquitin-independent **p53** degradation We now show that, like dicoumarol, several other coumarin and flavone inhibitors of NQO1 activity, which compete with NAD(P)H for binding to NQO1, induced ubiquitin-independent **p53** degradation and inhibited wild-type **p53**-mediated apoptosis. Although wild-type **p53** and several **p53 mutants** were sensitive to dicoumarol-induced degradation, the most frequent "hot-spot" **p53 mutants** in human cancer, **R175H**, R248H, and **R273H**, were resistant to dicoumarol-induced degradation, but remained sensitive to Mdm2-ubiquitin-mediated degradation The two alternative pathways for **p53** degradation thus have different **p53** structural requirements. Further mutational anal. showed that arginines at positions 175 and 248 were essential for dicoumarol-induced **p53** degradation NQO1 bound to wild-type **p53** and dicoumarol, which induced a conformational change in NQO1, inhibited this binding. Compared with wild-type **p53**, the hot-spot **p53** mutants showed increased binding to NQO1, which can explain their resistance to dicoumarol-induced degradation NQO1 thus has an important role in **stabilizing** hot-spot **p53** mutant proteins in human cancer.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 27 Nov 2003
ACCESSION NUMBER: 2003:926529 CAPLUS
DOCUMENT NUMBER: 140:57472
TITLE: Elevated levels of prostate-specific antigen (PSA) in prostate cancer cells expressing mutant **p53** is associated with tumor metastasis
AUTHOR(S): Downing, Sean; Bumak, Clare; Nixdorf, Sheri; Ow, Kim; Russell, Pamela; Jackson, Paul
CORPORATE SOURCE: Oncology Research Centre, Prince of Wales Hospital, Randwick, Australia
SOURCE: Molecular Carcinogenesis (2003), 38(3), 130-140
CODEN: MOCAE8; ISSN: 0899-1987
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The underlying basis for rising levels of prostate-specific antigen (PSA) in prostate cancer is not fully understood, but attention has turned to the possibility that loss of normal **p53** function might be directly involved. We have investigated the relationship between

p53 function and PSA expression using in vitro and in vivo approaches. Three prostate cancer-derived **p53 mutants** (F134L, M237L, **R273H**) were introduced into LNCaP prostate cancer cells and **stable** transfectants established. Expression of mutant **p53** was demonstrated by Western blot anal., inactivation of wtp53 function, and a loss of **p53**-dependent responses to DNA damage induced by UV-irradiation and cisplatin. Levels of PSA mRNA and secreted protein were determined by RT-PCR and Western blotting, resp. Serine protease activity was assessed using an esterase assay. In vivo effects of mutant **p53** expression were examined after orthotopic implantation into prostates of nude mice. Expression of all **p53** mutants was associated with elevated PSA mRNA and secreted PSA protein. In a representative line, mutant **p53** was also associated with increased PSA protease-like activity compared with a control line expressing wildtype **p53**. Overall PSA levels, and PSA levels in serum from mice bearing tumors derived from cells expressing mutant **p53**, were increased compared with levels in mice bearing tumors derived from control cells. In addition, the tumors derived from cells with mutant **p53** had increased vascularization and induced lymph node metastases. These data provide in vitro and in vivo support for the notion that **p53** mutations directly contribute to increased levels of serum PSA, and are associated with more aggressive tumors.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 01 Oct 2003
ACCESSION NUMBER: 2003:766871 CAPLUS
DOCUMENT NUMBER: 139:347259
TITLE: Conversion of Wild-type **p53** Core Domain into a Conformation that Mimics a Hot-spot Mutant
AUTHOR(S): Ishimaru, Daniella; Maia, Lenize F.; Maiolino, Larissa M.; Quesado, Pablo A.; Lopez, Priscila C. M.; Almeida, Fabio C. L.; Valente, Ana Paula; Silva, Jerson L.
CORPORATE SOURCE: Instituto de Ciencias Biomedicas, Centro Nacional de Ressonancia Magnetica Nuclear de Macromoleculas, Departamento de Bioquimica Medica, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, 21941-590, Brazil
SOURCE: Journal of Molecular Biology (2003), 333(2), 443-451
CODEN: JMOBAK; ISSN: 0022-2836
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The wild-type **p53** protein can be driven into a conformation corresponding to that adopted by structural mutant forms by heterodimerization with a mutant subunit. To seek partially folded states of the wild-type **p53** core domain (p53C) we used high hydrostatic pressure (HP) and subzero temps. Aggregation of the protein was observed in parallel with its pressure denaturation at 25 and 37°. However, when HP expts. were performed at 4°, the extent of denaturation and aggregation was significantly less pronounced. On the other hand, subzero temps. under pressure led to cold denaturation and yielded a non-aggregated, alternative conformation of p53C. NMR (1H15N-NMR) data

showed that the alternative p53C conformation resembled that of the hot-spot oncogenic **mutant R248Q**. This alternative state was as susceptible to denaturation and aggregation as the **mutant R248Q** when subjected to HP at 25°. Together these data demonstrate that wild-type p53C adopts an alternative conformation with a mutant-like **stability**, consistent with the dominant-neg. effect caused by many mutants. This alternative conformation is likely related to inactive forms that appear in vivo, usually driven by interaction with mutant proteins. Therefore, it can be a valuable target in the search for ways to interfere with protein misfolding and hence to prevent tumor development.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 23 Jun 2003
ACCESSION NUMBER: 2003:478413 CAPLUS
DOCUMENT NUMBER: 139:241840
TITLE: Kinetic Instability of **p53** Core Domain Mutants: Implications For Rescue By Small Molecules
AUTHOR(S): Friedler, Assaf; Veprintsev, Dmitry B.; Hansson, Lars O.; Fersht, Alan R.
CORPORATE SOURCE: Cambridge Centre for Protein Engineering, Medical Research Council Centre, Cambridge University Chemical Laboratory, Cambridge, CB2 2QH, UK
SOURCE: Journal of Biological Chemistry (2003), 278(26), 24108-24112
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Oncogenic mutations in the tumor suppressor protein **p53** are found mainly in its DNA-binding core domain. Many of these mutants are thermodynamically unstable at body temperature Here the authors show that these mutants also denature within minutes at 37°. The half-life (t1/2) of the unfolding of wild-type **p53** core domain was 9 min. Hot spot mutants denatured more rapidly with increasing thermodn. instability. The highly destabilized **mutant I195T** had a t1/2 of less than 1 min. The wild-type **p53**-(94-360) construct, containing the core and tetramerization domains, was more **stable**, with t1/2= 37 min at 37°, similar to full-length **p53**. After unfolding, the denatured proteins aggregated, the rate increasing with higher concns. of protein. A derivative of the **p53-stabilizing** peptide CDB3 significantly slowed down the unfolding rate of the **p53** core domain. Drugs such as CDB3, which rescue the conformation of unstable mutants of **p53**, have to act during or immediately after biosynthesis. They should maintain the mutant protein in a folded conformation and prevent its aggregation, allowing it enough time to reach the nucleus and bind its sequence-specific target DNA or the **p53** binding proteins that will **stabilize** it.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 04 Jun 2003
ACCESSION NUMBER: 2003:425714 CAPLUS
DOCUMENT NUMBER: 140:159220
TITLE: Rescuing the conformation of mutant **p53** core domain
AUTHOR(S): Friedler, Assaf; Hansson, Lars O.; Veprintsev, Dmitry B.; Freund, Stefan M. V.; Rippin, Thomas M.; Fersht, Alan R.
CORPORATE SOURCE: MRC Centre, Cambridge University Chemical Laboratory and Cambridge Centre for Protein Engineering, Cambridge, CB2 2QH, UK
SOURCE: Innovation and Perspectives in Solid Phase Synthesis & Combinatorial Libraries: Peptides, Proteins and Nucleic Acids--Small Molecule Organic Chemistry Diversity, Collected Papers, International Symposium, 7th, Southampton, United Kingdom, Sept. 18-22, 2001 (2002), Meeting Date 2001, 115-118. Editor(s): Epton, Roger. Mayflower Worldwide Ltd.: Kingswinford, UK. CODEN: 69DYT7; ISBN: 0-9515735-4-3
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Mutations in the tumor suppressor protein **p53** can, in principle, be rescued using a small mol. that binds the native, but not the denatured state. The equilibrium is then shifted towards the native state, resulting in **stabilization** and restoration of activity. The feasibility of this concept was demonstrated using peptides such as 9 amino acid residue peptide, CDB3, that binds to **p53** core domain and **stabilizes** it in vitro. Based on the crystal structure of the complex between **p53** and its binding protein 53BP2, the peptides derived from the three 53BP2 loops that bind **p53** core domain were designed and synthesized. In addition, peptides from the C-terminal and proline-rich domains of **p53**, which were suggested to bind the core domain, were synthesized. CDB3, as a peptide that globally **stabilizes p53** core domain, could restore DNA binding activity to the globally destabilized **mutant I195T**. Results showed that short peptides can be used to **stabilize** mutant **p53** and restore its DNA binding activity. CDB3 binds at the DNA binding site, but DNA binds **p53** tighter and thus can displace the peptide. CDB3 acts in the following mechanism: it binds globally destabilized mutants that are unable to bind DNA, and brings them to the stage where they can bind DNA, then DNA displaces the peptide and binds to the newly refolded mutant.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 02 Feb 2003
ACCESSION NUMBER: 2003:77898 CAPLUS
DOCUMENT NUMBER: 138:233667
TITLE: Structure, Function, and Aggregation of the Zinc-Free Form of the **p53** DNA Binding Domain
AUTHOR(S): Butler, James S.; Loh, Stewart N.
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, State University of New York Upstate Medical

University, Syracuse, NY, 13210, USA
SOURCE: Biochemistry (2003), 42(8), 2396-2403
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **p53** DNA binding domain (DBD) contains a single bound zinc ion that is essential for activity. Zinc remains bound to wild-type DBD at temps. below 30°; however, it rapidly dissocs. at physiol. temperature The resulting zinc-free protein (apoDBD) is folded and **stable**. NMR spectra reveal that the DNA binding surface is altered in the absence of Zn2+. Fluorescence anisotropy studies show that Zn2+ removal abolishes site-specific DNA binding activity, although full nonspecific DNA binding affinity is retained. Surprisingly, the majority of tumorigenic mutations that destabilize DBD do not appreciably destabilize apoDBD. The **R175H mutation** instead substantially accelerates the rate of Zn2+ loss. A considerable fraction of cellular **p53** may therefore exist in the folded zinc-free form, especially when tumorigenic mutations are present. ApoDBD appears to promote aggregation of zinc-bound DBD via a nucleation-growth process. These data provide an explanation for the dominant neg. phenotype exhibited by many mutations. Through a combination of induced **p53** aggregation and diminished site-specific DNA binding activity, Zn2+ loss may represent a significant inactivation pathway for **p53** in the cell.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 29 Apr 2002
ACCESSION NUMBER: 2002:317812 CAPLUS
DOCUMENT NUMBER: 137:165125
TITLE: Factors governing loss and rescue of DNA binding upon single and double mutations in the **p53** core domain
AUTHOR(S): Wright, Jon D.; Noskov, Sergey Yu; Lim, Carmay
CORPORATE SOURCE: Institute of Biomedical Sciences, Academia Sinica, Taipei, 11529, Taiwan
SOURCE: Nucleic Acids Research (2002), 30(7), 1563-1574
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The mutation of R273→H in the **p53** core domain (**p53**-CD) is one of the most common mutations found in human cancers. Although the 273H **p53**-CD retains the wild-type conformation and **stability**, it lacks sequence-specific DNA binding, a transactivation function and growth suppression. However, mutating T284→R in the 273H **p53**-CD restores the DNA binding affinity, and transactivation and tumor suppressor functions. Since X-ray/NMR structures of DNA-free or DNA-bound mutant **p53** -CD mols. are unavailable, the factors governing the loss and rescue of sequence-specific DNA binding in the 273H and 273H+284R **p53**-CD, resp., are unclear. Hence, we have carried out mol. dynamics (MD) simulations of the wild-type, single mutant and double mutant **p53** -CD, free and DNA bound, in the presence of explicit water mols. Based on the MD structures, the DNA-binding free energy of each **p53** mol.

has been computed and decomposed into component energies and contributions from the interface residues. The wild-type and mutant **p53**-CD MD structures were found to be consistent with the antibody-binding, X-ray and NMR data. The predicted DNA binding affinity and specificity of both mutant **p53**-CDs were also in accord with exptl. data. The non-detectable DNA binding of the 273H **p53**-CD is due mainly to the disruption of a hydrogen-bonding network involving R273, D281 and R280, leading to a loss of major groove binding by R280 and K120. The restoration of DNA binding affinity and specificity of the 273H+284R **p53**-CD is due mainly to the introduction of another DNA-binding site at position 284, leading to a recovery of major groove binding by R280 and K120. The important role of water mols. and the DNA major groove conformation as well as implications for structure-based linker rescue of the 273H **p53**-CD DNA-binding affinity are discussed.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 22 Apr 2002
ACCESSION NUMBER: 2002:298460 CAPLUS
DOCUMENT NUMBER: 137:210559
TITLE: Characterization of the **p53**-rescue drug CP-31398 in vitro and in living cells
AUTHOR(S): Rippin, Thomas M.; Bykov, Vladimir J. N.; Freund, Stefan M. V.; Selivanova, Galina; Wiman, Klas G.; Fersht, Alan R.
CORPORATE SOURCE: MRC Centre, Cambridge University Chemical Laboratory and Cambridge Center for Protein Engineering, Cambridge, CB2 2QH, UK
SOURCE: Oncogene (2002), 21(14), 2119-2129
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The Pfizer compound CP-31398 has been reported to **stabilize** the core domain of the tumor suppressor **p53** in vitro and be an effective anti-cancer drug by virtue of rescuing destabilized mutants of **p53**. The authors did not detect any interaction between the **p53** core domain and CP-31398 in vitro by a wide range of quant. biophys. techniques over a wide range of conditions. CP-31398 did not **stabilize p53** in the authors' expts. However, the authors found that CP-31398 intercalated with DNA and also altered and destabilized the DNA-**p53** core domain complex. The authors analyzed by NMR TROSY the interaction of the domain with a DNA oligomer and identified the changes in the complex on the binding of CP-31398. CP-31398 also decreased sequence-specific DNA binding of wild-type **p53** and His 273 mutant **p53**. CP-31398 had a non-specific toxic effect independent of mutant **p53** expression in several cell lines carrying Tet-regulated mutant **p53**. CP-31398 caused a small increase in MDM-2 expression and a more pronounced **p53** -independent increase in Bax expression. CP-31398 did, however, induce the PAb1620 epitope (characteristic of native **p53**) in cells expressing His 175 mutant **p53**. This was prevented by cycloheximide, suggesting that any **stabilizing** action of CP-31398 would have to be on newly synthesized **p53**. One of the unstable **mutants** that was reported to have been rescued by

CP-31398, **R249S**, does not bind DNA when folded at lower temps.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 15 Feb 2002
ACCESSION NUMBER: 2002:121133 CAPLUS
DOCUMENT NUMBER: 136:292597
TITLE: A peptide that binds and **stabilizes** **p53** core domain: chaperone strategy for rescue of oncogenic mutants
AUTHOR(S): Friedler, Assaf; Hansson, Lars O.; Veprintsev, Dmitry B.; Freund, Stefan M. V.; Rippin, Thomas M.; Nikolova, Penka V.; Proctor, Mark R.; Rudiger, Stefan; Fersht, Alan R.
CORPORATE SOURCE: Medical Research Council Centre, Cambridge University Chemical Laboratory and Cambridge Centre for Protein Engineering, Cambridge, CB2 2QH, UK
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2002), 99(2), 937-942
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Conformationally compromised oncogenic mutants of the tumor suppressor protein **p53** can, in principle, be rescued by small mols. that bind the native, but not the denatured state. We describe a strategy for the rational search for such mols. A nine-residue peptide, CDB3, which was derived from a **p53** binding protein, binds to **p53** core domain and **stabilizes** it in vitro. NMR studies showed that CDB3 bound to **p53** at the edge of the DNA binding site, partly overlapping it. The fluorescein-labeled peptide, FL-CDB3, binds wild-type **p53** core domain with a dissociation constant of 0.5 μM, and raises the apparent melting temps. of wild-type and a representative oncogenic mutant, R2495 core domain, gadd45 DNA competes with CDB3 and displaces it from its binding site. But this competition does not preclude CDB3 from being a lead compound CDB3 may act as a "chaperone" that maintains existing or newly synthesized destabilized **p53** mutants in a native conformation and then allows transfer to specific DNA, which binds more tightly. Indeed, CDB3 restored specific DNA binding activity to a highly destabilized **mutant I195T** to close to that of wild-type level.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 09 Jul 2001
ACCESSION NUMBER: 2001:493520 CAPLUS
DOCUMENT NUMBER: 136:241188
TITLE: Various forms of mutant **p53** confer sensitivity to cisplatin and doxorubicin in bladder cancer cells
AUTHOR(S): Chang, Fu-Lin; Lai, Ming-Derg
CORPORATE SOURCE: Department of Biochemistry, College of Medicine, National Cheng Kung University and Department of Industrial Safety and Hygiene, Chung Hwa Institute of

Technology, Tainan, Taiwan
SOURCE: Journal of Urology (Hagerstown, MD, United States) (2001), 166(1), 304-310
CODEN: JOURAA; ISSN: 0022-5347
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purposes: The nature of **p53** mutation has been reported to affect cellular responses to chemotherapy. We characterized the impact of **p53** mutations on drug resistance in bladder cancer cells. Materials and Methods: Various human **p53 mutants** (V143A, V173L, H179Q, N247I and **R273H**) were introduced to the TCC-SUP bladder carcinoma cell line to establish **stable** transfectants. The expression of mutant **p53** was demonstrated by reverse transcriptase-polymerase chain reaction and immunocytochem. anal. The sensitivity to cisplatin and doxorubicin in these transfectants was determined by trypan blue exclusion. Cell death mediated by cisplatin and doxorubicin was characterized by terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick end-labeling anal., Hoechst 33258 staining and annexin-V binding assay. Results: The expression of all forms of mutant **p53** protein except p53His273 enhanced sensitivity to cisplatin and doxorubicin. The chemosensitivity of p53His273 transfectants is similar to that of parental TCC-SUP and control transfectants. Cisplatin induced cell death undergoes apoptosis, as demonstrated by Hoechst staining, annexin-V assay and terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick end-labeling, resp. In contrast, doxorubicin induced cell death probably occurs through a non-apoptotic pathway. Conclusions: These results indicated that the nature of **p53** mutations may effect the cellular response to anticancer drugs and many forms of mutant **p53** protein may enhance chemosensitivity through apoptotic or non-apoptotic pathways in bladder cancer cells.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 28 Jun 2001
ACCESSION NUMBER: 2001:465094 CAPLUS
DOCUMENT NUMBER: 135:193334
TITLE: ZBP-89 promotes growth arrest through **stabilization** of **p53**
AUTHOR(S): Bai, Longchuan; Merchant, Juanita L.
CORPORATE SOURCE: Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA
SOURCE: Molecular and Cellular Biology (2001), 21(14), 4670-4683
CODEN: MCEBD4; ISSN: 0270-7306
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Transcription factor **p53** can induce growth arrest and/or apoptosis in cells through activation or repression of downstream target genes. Recently, we reported that ZBP-89 cooperates with histone acetyltransferase coactivator p300 in the regulation of p21waf1, a cyclin-dependent kinase inhibitor whose associated gene is a target gene of **p53**. Therefore, we examined whether ZBP-89 might also inhibit cell

growth by activating **p53**. In the present study, we demonstrate that elevated levels of ZBP-89 induce growth arrest and apoptosis in human gastrointestinal cell lines. The ZBP-89 protein accumulated within 4 h, and the **p53** protein accumulated within 16 h, of serum starvation without changes in p14ARF levels, demonstrating a physiol. increase in the cellular levels of these two proteins. Overexpression of ZBP-89 **stabilized** the **p53** protein and enhanced its transcriptional activity through direct protein-protein interactions. The DNA binding and C-terminal domains of **p53** and the zinc finger domain of ZBP-89 mediated the interaction. A point **mutation** in the **p53** DNA binding domain, **R273H**, greatly reduced ZBP-89-mediated **stabilization** but not their phys. interaction. Furthermore, ZBP-89 formed a complex with **p53** and MDM2 and therefore did not prevent the MDM2-**p53** interaction. However, heterokaryon assays demonstrated that ZBP-89 retained **p53** in the nucleus. Collectively, these data indicate that ZBP-89 regulates cell proliferation in part through its ability to directly bind the **p53** protein and retard its nuclear export. Our findings further our understanding of how ZBP-89 modulates cell proliferation and reveals a novel mechanism by which the **p53** protein is **stabilized**

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REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 07 Mar 2001
ACCESSION NUMBER: 2001:160241 CAPLUS
DOCUMENT NUMBER: 135:222217
TITLE: p73 is transcriptionally regulated by DNA damage, **p53**, and p73
AUTHOR(S): Chen, Xinbin; Zheng, Yiman; Zhu, Jianhui; Jiang, Jieyuan; Wang, Jian
CORPORATE SOURCE: Institute of Molecular Medicine and Genetics, Medical College of Georgia, Augusta, GA, 30912, USA
SOURCE: Oncogene (2001), 20(6), 769-774
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB P73 is a member of the **p53** family. Recent studies have shown that DNA damage can **stabilize** p73 protein and enhance p73-mediated apoptosis in a c-Abl dependent manner. To determine what regulates p73 transcriptionally, we analyzed the expression of p73 in several cell lines following genotoxic stresses. We found that p73 is induced in certain cell lines when treated with therapeutic DNA damaging agents. We also found that **p53** and p73, but not **mutant p53 (R249S)** and p73β292, directly induce the expression of the p73 gene. In addition, we found one potential **p53** -binding site in the promoter of the p73 gene. This binding site is responsive to **p53**, p73, and DNA damage. Taken together, these data suggest that p73 is transcriptionally regulated by DNA damage and **p53**, and is autoregulated.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 27 Feb 2001
ACCESSION NUMBER: 2001:141119 CAPLUS
DOCUMENT NUMBER: 134:308356
TITLE: **p53** associates with and targets ΔNp63 into a protein degradation pathway
AUTHOR(S): Ratovitski, Edward A.; Patturajan, Meera; Hibi, Kenji; Trink, Barry; Yamaguchi, Kengo; Sidransky, David
CORPORATE SOURCE: Department of Otolaryngology-Head and Neck Surgery, Division of Head and Neck Cancer Research, The Johns Hopkins University School of Medicine, Baltimore, MD, 21205-2196, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(4), 1817-1822
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A human **p53** homolog, p63 (p40/p51/p73L/CUSP) that maps to the chromosomal region 3q27-29 was found to produce a variety of transcripts that encode DNA-binding proteins with and without a trans-activation domain (TA- or ΔN-, resp.). The p63 gene locus was amplified in squamous cell carcinoma, and overexpression of ΔNp63 (p40) led to increased growth of transformed cells in vitro and in vivo. Moreover, p63-null mice displayed abnormal epithelial development and germ-line human mutations were found to cause ectodermal dysplasia. The authors now demonstrate that certain p63 isotypes form complexes with **p53**. **P53 mutations** **R175H** or R248W abolish the association of **p53** with p63, whereas V143A or **R273H** has no effect. Deletion studies suggest that the DNA-binding domains of both **p53** and p63 mediate the association Overexpression of wild type but not **mutant** (**R175H**) **p53** results in the caspase-dependent degradation of certain ΔNp63 proteins (p40 and ΔNp63α). The association between **p53** and ΔNp63 supports a previously unrecognized role for **p53** in regulation of ΔNp63 **stability**. The ability of **p53** to mediate ΔNp63 degradation may balance the capacity of ΔNp63 to accelerate tumorigenesis or to induce epithelial proliferation.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 13 Feb 2000
ACCESSION NUMBER: 2000:100300 CAPLUS
DOCUMENT NUMBER: 132:235186
TITLE: Mechanism of rescue of common **p53** cancer mutations by second-site suppressor mutations
AUTHOR(S): Nikolova, Penka V.; Wong, Kam-Bo; DeDecker, Brian; Henckel, Julia; Fersht, Alan R.
CORPORATE SOURCE: Cambridge University Chemical Laboratory and Cambridge Centre for Protein Engineering, MRC Centre, Cambridge, CB2 2QH, UK
SOURCE: EMBO Journal (2000), 19(3), 370-378
CODEN: EMJODG; ISSN: 0261-4189
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The core domain of **p53** is extremely susceptible to mutations that lead to loss of function. We analyzed the **stability** and DNA-binding activity of such mutants to understand the mechanism of second-site suppressor mutations. Double-**mutant** cycles show that N239Y and N268D act as "global **stability**" suppressors by increasing the **stability** of the cancer **mutants** **G245S** and V143A-the free energy changes are additive. Conversely, the suppressor H168R is specific for the **R249S** **mutation**: despite destabilizing wild type, H168R has virtually no effect on the **stability** of **R249S**, but restores its binding affinity for the gadd45 promoter. NMR structural comparisons of R249S/H168R and R249S/T123A/H168R with wild type and R249S show that H168R reverts some of the structural changes induced by R249S. These results have implications for possible drug therapy to restore the function of tumorigenic **mutants** of **p53**: the function of **mutants** such as V143A and **G245S** is theor. possible to restore by small mols. that simply bind to and hence **stabilize** the native structure, whereas **R249S** requires alteration of its **mutant** native structure.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 14 May 1999
ACCESSION NUMBER: 1999:298113 CAPLUS
DOCUMENT NUMBER: 131:156276
TITLE: Modulation of wild-type **p53** activity by **mutant p53 R273H** depends on the **p53** responsive element (p53RE). A comparative study between the p53REs of the MDM2, WAFI/Cip1 and Bax genes in the lung cancer environment
AUTHOR(S): Zacharatos, P. V.; Gorgoulis, V. G.; Kotsinas, A.; Manolis, E. N.; Liloglou, T.; Rassidakis, A. N.; Kanavaros, P.; Field, J. D.; Halazonetis, T.; Kittas, Ch.
CORPORATE SOURCE: Department of Histology and Embryology, School of Medicine, University of Athens, Athens, Greece
SOURCE: Anticancer Research (1999), 19(1A), 579-588
CODEN: ANTRD4; ISSN: 0250-7005
PUBLISHER: International Institute of Anticancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Wild-type (weight) **p53** is a tumor-suppressor protein which acts via transcriptional and transcriptional-independent mechanisms. The transcriptional function of **p53** is mediated by specific responsive elements (REs). The MDM2, WAF1/Cip1, and Bax genes possess p53REs and their activation by wt **p53** induces cell cycle progression, arrest, and programmed cell death (apoptosis), resp. Mutations of the **p53** gene are detected in more than 50% of the human malignant tumors. **p53** mutants seem to have a more **stable** conformation and are suggested to exert dominant-neg. inhibition of wt **p53** in cells containing both wt and mutant (mt) alleles. However, recent studies show that certain mt **p53** proteins possess a "gain of function" phenotype. In the present study, the effects of the second most-frequent **p53 mutant** **R273H** on the p53REs of the MDM2, WAF1/Cip1, and Bax genes in the

H1299 non-small-cell lung carcinoma cell line were examined Although mt **p53** R273H alone was unable to bind and transactivate the corresponding p53REs, it enhanced the MDM2-p53RE-mediated gene transcription of wt **p53** (pos.-dominant effect) and prevented the wt **p53** transactivation of the p53REs of WAF1/Cip1 and Bax genes (neg.-dominant effect). Apparently, in the appropriate environment, differential transcription of critical **p53** target genes by certain **p53** mutant proteins may illustrate another mechanism implicated in tumor development.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 11 May 1998
ACCESSION NUMBER: 1998:266241 CAPLUS
DOCUMENT NUMBER: 129:37195
TITLE: Adenovirus type 12-induced fragility of the human RNU2 locus requires **p53** function
AUTHOR(S): Li, Zengji; Yu, Adong; Weiner, Alan M.
CORPORATE SOURCE: Departments of Molecular Biophysics and Biochemistry and of Genetics, Yale University, New Haven, CT, 06520-8114, USA
SOURCE: Journal of Virology (1998), 72(5), 4183-4191
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Adenovirus type 12 (Ad12) infection of human cells induces four chromosomal fragile sites corresponding to the U1 small nuclear RNA (snRNA) genes (the RNU1 locus), the U2 snRNA genes (RNU2), the U1 snRNA pseudogenes (PSU1), and the 5S rRNA genes (RN5S). Ad12-induced fragility of the RNU2 locus requires U2 snRNA transcriptional regulatory elements and viral early functions but not viral replication or integration, or chromosomal sequences flanking the RNU2 locus. We now show that Ad12 cannot induce the RNU1, RNU2, or PSU1 fragile sites in Saos-2 cells lacking the **p53** and retinoblastoma (Rb) proteins but viral induction of fragility is rescued in these cells when the expression of wild-type **p53** or selected hot-spot **mutants** (i.e., V143A, **R175H**, R248W, and **R273H**) is restored by transient expression or **stable** retroviral transduction. We also observed weak constitutive fragility of the RNU1 and RNU2 loci in cells belonging to xeroderma pigmentosum complementation groups B and D (XPB and XPD) which are partially defective in the ERCC2 (XPD) and ERCC3 (XPB) helicase activities shared between the repairosome and the RNA polymerase II basal transcription factor TFIIH. We propose a model for Ad12-induced chromosome fragility in which interaction of **p53** with the Ad12 E1B 55-kDa transforming protein (and possibly E4orf6) induces a **p53** grain of function which ultimately perturbs the RNA polymerase II basal transcription apparatus The **p53** gain of function could interfere with chromatin condensation either by blocking mitotic shutdown of U1 and U2 mRNA transcription or by phenocopying global or local DNA damage. Specific fragilization of the RNU1, RNU2, and PSU1 loci could reflect the usually high local concentration of strong transcription units or the specialized nature of the U1 and U2 snRNA transcription apparatus

REFERENCE COUNT: 99 THERE ARE 99 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 02 May 1998
ACCESSION NUMBER: 1998:249758 CAPLUS
DOCUMENT NUMBER: 129:23853
TITLE: Genetic selection of intragenic suppressor mutations that reverse the effect of common **p53** cancer mutations
AUTHOR(S): Brachmann, Rainer K.; Yu, Kexin; Eby, Yolanda; Pavletich, Nikola P.; Boeke, Jef D.
CORPORATE SOURCE: Department of Molecular Biology and Genetics, The Johns Hopkins University School of Medicine, Baltimore, MD, 21205, USA
SOURCE: EMBO Journal (1998), 17(7), 1847-1859
CODEN: EMJODG; ISSN: 0261-4189
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several lines of evidence suggest that the presence of the wild-type tumor suppressor gene **p53** in human cancers correlates well with successful anti-cancer therapy. Restoration of wild-type **p53** function to cancer cells that have lost it might therefore improve treatment outcomes. Using a systematic yeast genetic approach, we selected second-site suppressor mutations that can overcome the deleterious effects of common **p53** cancer mutations in human cells. We identified several suppressor **mutations** for the V143A, **G245S** and **R249S** cancer **mutations**. The beneficial effects of these suppressor mutations were demonstrated using mammalian reporter gene and apoptosis assays. Further expts. showed that these suppressor mutations could override addnl. **p53** cancer mutations. The mechanisms of such suppressor mutations can be elucidated by structural studies, ultimately leading to a framework for the discovery of small mols. able to **stabilize p53** mutants.
REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 17 Jan 1998
ACCESSION NUMBER: 1998:26794 CAPLUS
DOCUMENT NUMBER: 128:126436
TITLE: Thermodynamic **stability** of wild-type and mutant **p53** core domain
AUTHOR(S): Bullock, Alex N.; Henckel, Julia; DeDecker, Brian S.; Johnson, Christopher M.; Nikolova, Penka V.; Proctor, Mark R.; Lane, David P.; Fersht, Alan R.
CORPORATE SOURCE: Medical Research Council Centre, Cambridge University Chemical Laboratory, Cambridge, CB2 2QH, UK
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1997), 94(26), 14338-14342
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Some 50% of human cancers are associated with mutations in the core domain of

the tumor suppressor **p53**. Many mutations are thought just to destabilize the protein. To assess this and the possibility of rescue, the authors have set up a system to analyze the **stability** of the core domain and its mutants. The use of differential scanning colorimetry or spectroscopy to measure its melting temperature leads to irreversible denaturation and aggregation and so is useful as only a qual. guide to **stability**. There are excellent two-state denaturation curves on the addition of urea that may be analyzed quant. One Zn2+ ion remains tightly bound in the holoform of **p53** throughout the denaturation curve. The **stability** of wild type is 6.0 kcal (1 kcal = 4.18 kJ)/mol at 25° and 9.8 kcal/mol at 10°. The oncogenic **mutants R175H**, C242S, **R248Q**, **R249S**, and **R273H** are destabilized by 3.0, 2.9, 1.9, 1.9, and 0.4 kcal/mol, resp. Under certain denaturing conditions, the wild-type domain forms an aggregate that is relatively highly fluorescent at 340 nm on excitation at 280 nm. The destabilized mutants give this fluorescence under milder denaturation conditions.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, CANCERLIT' ENTERED AT 15:10:34 ON 03 MAR 2005)

L11 92 S L9
L12 24 DUP REM L11 (68 DUPLICATES REMOVED)

L12 ANSWER 1 OF 24 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2004531006 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15308639
TITLE: CP-31398 restores DNA-binding activity to mutant **p53** in vitro but does not affect **p53** homologs p63 and p73.
AUTHOR: Demma Mark J; Wong Serena; Maxwell Eugene; Dasmahapatra Bimalendu
CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, New Jersey 07033, USA.
SOURCE: Journal of biological chemistry, (2004 Oct 29) 279 (44) 45887-96. Electronic Publication: 2004-08-11. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 20041026
Last Updated on STN: 20041219
Entered Medline: 20041130

AB The **p53** protein plays a major role in the maintenance of genome **stability** in mammalian cells. Mutations of **p53** occur in over 50% of all cancers and are indicative of highly aggressive cancers that are hard to treat. Recently, there has been a high degree of interest in therapeutic approaches to restore growth suppression functions to mutant **p53**. Several compounds have been reported to restore wild type function to mutant **p53**. One such compound, CP-31398, has been shown effective in vivo, but questions have arisen to whether it actually affects **p53**. Here we show that mutant **p53**, isolated from cells treated with CP-31398, is capable of binding to

p53 response elements in vitro. We also show the compound restores DNA-binding activity to mutant **p53** in cells as determined by a chromatin immunoprecipitation assay. In addition, using purified **p53** core domain from two different hotspot **mutants** (**R273H** and **R249S**), we show that CP-31398 can restore DNA-binding activity in a dose-dependent manner. Using a quantitative DNA binding assay, we also show that CP-31398 increases significantly the amount of mutant **p53** that binds to cognate DNA (B(max)) and its affinity (K(d)) for DNA. The compound, however, does not affect the affinity (K(d) value) of wild type **p53** for DNA and only increases B(max) slightly. In a similar assay PRIMA1 does not have any effect on **p53** core DNA-binding activity. We also show that CP-31398 had no effect on the DNA-binding activity of **p53** homologs p63 and p73.

L12 ANSWER 2 OF 24 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004239635 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15004724
TITLE: Mutant **p53** expression enhances drug resistance in a hepatocellular carcinoma cell line.
AUTHOR: Chan Kin-Tak; Lung Maria Li
CORPORATE SOURCE: Department of Biology, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong (SAR), People's Republic of China.
SOURCE: Cancer chemotherapy and pharmacology, (2004 Jun) 53 (6) 519-26. Electronic Publication: 2004-03-04. Journal code: 7806519. ISSN: 0344-5704.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20040513
Last Updated on STN: 20040629
Entered Medline: 20040628

AB Chemoresistance is a major problem in the treatment of hepatocellular carcinoma. Certain **p53** mutants may enhance drug resistance in cancer cells. To determine whether two frequently occurring **p53 mutants, R248Q** and R273C, would increase the drug resistance of liver cancer cells, **stable** cell lines expressing these specific **p53 mutants** were established by transfecting the **p53**-null Hep3B cells with **mutant p53** expression vectors, and then treating them with the anticancer drugs doxorubicin and paclitaxel. The cells expressing the **p53 mutant, R248Q**, but not R273C, displayed cross-resistance to both drugs, in contrast to the control cells expressing the vector alone. Moreover, both the expression and the activity of the multiple drug resistance gene product, P-glycoprotein, were elevated in **p53 mutant R248Q**-expressing cells. Reduced uptake of doxorubicin was also observed in the R248Q-expressing cells. These results suggest that expression of the **p53 mutant, R248Q**, in liver cancer cells may enhance their drug resistance and that upregulation of P-glycoprotein activity may contribute to this protective effect.

L12 ANSWER 3 OF 24 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-663348 [62] WPIDS
DOC. NO. CPI: C2003-180150
TITLE: Nucleic acid molecule encoding tumor suppressor protein, useful for treating cancer, comprises intragenic suppressor mutation suppressing mutation of transcription factor in human cancers when the mutations are in a cis configuration.
DERWENT CLASS: B04
INVENTOR(S): BRACHMANN, R K
PATENT ASSIGNEE(S): (UNIW) UNIV WASHINGTON
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003061603	A2	20030731	(200362)*	EN	27

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

AU 2003206373	A1	20030902	(200422)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003061603	A2	WO 2003-US24	20030115
AU 2003206373	A1	AU 2003-206373	20030115

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2003206373	A1	Based on	WO 2003061603

PRIORITY APPLN. INFO: US 2002-348394P 20020116
AN 2003-663348 [62] WPIDS
AB WO2003061603 A UPAB: 20031001
NOVELTY - A nucleic acid molecule (A1) encoding human transcription factor and tumor suppressor protein (**p53**) comprises at least one intragenic suppressor mutation capable of suppressing a mutation of human **p53**, which occurs in human cancers when the intragenic suppressor and cancer mutations are present in a cis configuration.

DETAILED DESCRIPTION - A nucleic acid molecule (A1) encoding human **p53** comprises at least one intragenic suppressor mutation capable of suppressing a mutation of human **p53** which occurs in human cancers when the intragenic suppressor and cancer mutations are present in a cis configuration. The intragenic suppressor mutation is T81S, A83V, P87R, Q100L, Q100R, Q104P, F113L, L114V, T118M, V122I, C124S, K139R, Q144L, W146R, Q165L, V172I, H178Y, S183T, A189V, F212L, E224G, S227P, S227T, D228N, D228A, D228E, C229W, T230S, T231I, I232V, H233R, H233Y, Y234F, N235K, N235S, Y236N, N239M, N239W, N239L, N239F, N239R, N239H, S240Q, S240T, S240R, D281G, E285G, E285K, E294G, G325R, E343V, E346G

and/or D352G.

INDEPENDENT CLAIMS are also included for:

(1) A nucleic acid molecule (B1) encoding human **p53** comprises a set of at least one intragenic suppressor mutation, capable of suppressing a mutation of human **p53** which occurs in human cancers when the intragenic suppressor and cancer mutations are present in a cis configuration. The set is selected from F113L, L114V+T123P+V172I+A189V, T123P+A189V, S227P+N239Y, T118M+H168R, V122I+C124S+H168R, T123A+H168R, K139R+H168R+N239Y, H168R+T231I, T123A+S240R, H178Y+S240R, D281G+E285G+G325R+E343V, E285K+D352G, E285K+E294G+E346G, T81S+A83V+S240R, P87R+Q100L+Q104P+Q144L+S240R, Q100R+W146R+S240R, Q165L+F212L+S240R, S183T+S240R, E224G+S240R, S240R, D228A+N235K+N239M, D228E+N235K+Y236N+N239L, I232V+H233R+Y234F+N235K+N239L, N235K+S240T, Y234F+N239L, N235K+N239R, H233Y+N239Y, N239F, N239Y+S240Q, H233Y+N235K+N239Y, N235K+N239Y, N235S+N239Y+S240N, D228N+N239Y, N235K+N239W, D228E+N239Y, N235K+S240N, N239W, T230S+N239Y, S227T+N235K+N239Y, H233R+N235S+N239R+S240R, N239R, N239R+S240R, C229W+N239R+S240R, N239L+S240R, N239F+S240R, I232V+N239H+S240R, D228E+C229W+N235K+ N239Y+S240R and/or N239Y+S240R;

(2) A human **p53** protein comprising the intragenic suppressor mutation or the set comprising at least one intragenic suppressor mutation;

(3) A cell comprising (A1), (B1) or human **p53** protein; and

(4) A human **p53** polypeptide comprising a portion of human **p53** protein comprising residues 94-292, and at least one of the intragenic suppressor mutation or the set of the intragenic suppressor mutations.

ACTIVITY - Cytostatic; Gene therapy.

No biological data available.

MECHANISM OF ACTION - None given.

USE - The nucleic acids encapsulated or carried into vectors are used in gene therapy for the treatment of cancer. The **p53** molecules or polypeptides are used as cancer therapeutics, and for protein crystallography to determine a protein **stabilization** mechanism.

ADVANTAGE - The **p53** suppressor mutations are resistant to the dominant-negative effect of **p53** cancer mutants, and are efficient in inducing cell cycle arrest and apoptosis for the treatment of cancer.

Dwg.0/3

L12 ANSWER 4 OF 24 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER:	2003-256537 [25] WPIDS
DOC. NO. NON-CPI:	N2003-203483
DOC. NO. CPI:	C2003-066578
TITLE:	Novel **stabilizing** molecule which binds to a site that partially overlaps a functional site of polypeptide and **stabilizes** native state of polypeptide, but not denatured state of polypeptide, useful for treating cancer.
DERWENT CLASS:	B04 D16 S03
INVENTOR(S):	FERSHT, A; FRIEDLER, A
PATENT ASSIGNEE(S):	(MEDI-N) MEDICAL RES COUNCIL
COUNTRY COUNT:	102

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 2003014144 A2 20030220 (200325)* EN 73
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
EP 1414846 A2 20040506 (200430) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
AU 2002319540 A1 20030224 (200461)
US 2005008653 A1 20050113 (200506)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003014144	A2	WO 2002-GB3668	20020809
EP 1414846	A2	EP 2002-749128	20020809
		WO 2002-GB3668	20020809
AU 2002319540	A1	AU 2002-319540	20020809
US 2005008653	A1 CIP of	WO 2002-GB3668	20020809
		US 2004-775679	20040210

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1414846	A2 Based on	WO 2003014144
AU 2002319540	A1 Based on	WO 2003014144

PRIORITY APPLN. INFO: GB 2002-10740 20020510; GB 2001-19557 20010810; GB 2001-27917 20011121

AN 2003-256537 [25] WPIDS

AB WO2003014144 A UPAB: 20030416

NOVELTY - A **stabilizing** molecule (I) which binds to and **stabilizes** the native state of a polypeptide, but not a denatured state of the polypeptide, in which the **stabilizing** molecule binds to a site which at least partially overlaps a functional site of the polypeptide, and in which the **stabilizing** molecule does not consist of a natural binding partner of the polypeptide, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) identifying (I) capable of **stabilizing** a polypeptide in which the polypeptide may be reversibly denatured so that it exists in a native state and a denatured state, comprising:

(a) providing a native state of the polypeptide comprising a functional site;

(b) exposing the polypeptide to a candidate **stabilizing** molecule;

(c) selecting a candidate **stabilizing** molecule which binds to the site which at least partially overlaps a functional site of the native state of the polypeptide; and

(d) determining whether the binding **stabilizes** the native

state of the polypeptide; or

(2) identifying (I) capable of **stabilizing** a polypeptide in which the polypeptide may be reversibly denatured so that it exists in a native state and a denatured state, comprising:

(a) identifying a functional site of the polypeptide;

(b) providing the polypeptide fragment comprising the functional site;

(c) selecting a candidate **stabilizing** molecule which binds to the polypeptide fragment at a site which at least partially overlaps a functional site; and

(d) determining whether the selected candidate **stabilizing** molecule **stabilizes** a native state of a polypeptide;

(3) a **stabilizing** molecule capable of **stabilizing** the polypeptide, identified by the method of (2); and

(4) a pharmaceutical composition comprising (I), together with a carrier, diluent or excipient.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Apoptosis inducer.

The apoptosis-inducing effects of FL-CD3 on cell cycle was tested. Tumor cells were treated with 10 micro g/ml of peptide and the cell cycle distribution and cell death (as subG1 fraction) 24 hours post treatment was analyzed using fluorescence activated cell sorting (FACS) analysis. The percentage of dead cells was determined by trypan blue exclusion, the number of dead cells in H1299-His175 cells before treatment was 5 %, after treatment 37 %; in control H1299 (**p53**-), before 3 % after treatment 11 %; in Saos-2 His273 cells, before 3 %, after 28 %; in control Saos-2(**p53**-), before treatment 3 %, after 13 %. From the results of this experiment, it was clear that CDB3 peptide induced apoptosis in tumor cells in **p53**-dependent manner. There was difference between **p53**-positive and **p53**-negative cells. Surprisingly, no growth arrest was detected.

USE - (I) is useful for **stabilizing** the native state of a polypeptide which is reversibly denatured so that it exists in a native state and a denatured state, in which the **stabilizing** molecule does not bind to the polypeptide in its denatured state. (I) is useful for increasing the concentration of a native state of a reversibly denatured polypeptide in a system which comprises a polypeptide in a first native state and a second denatured state, which involves providing (I) which binds to the polypeptide at a site which at least partially overlaps with a functional site in the first native state and thereby **stabilizing** the first native state of the polypeptide, and allowing the **stabilizing** molecule to bind to the polypeptide. (I) is also useful for restoring a wild type phenotype of an organism comprising a mutation in a polypeptide, in which the mutation leads to denaturation of the polypeptide and a mutant phenotype, which involves exposing the organism or its part to (I). (I) is useful for treating a disease in a patient, caused by or associated with a mutation in a polypeptide which leads to denaturation of the polypeptide. (I) is not a natural binding partner of the polypeptide, and consists of fragment of natural binding partner of the polypeptide. (I) is a polypeptide engineered to include a polypeptide binding domain, preferably a binding loop, of a natural binding partner of the polypeptide. (I) is exposed to polypeptide or the system in presence of a natural binding partner of the polypeptide. The affinity of binding between **stabilizing** molecule and the polypeptide or site is less than the affinity of a natural binding partner of the polypeptide and the polypeptide or the

binding site. The binding between the **stabilizing** molecule and the binding site **stabilizes** the polypeptide to enable binding between the polypeptide and the natural binding partner, and the binding between the polypeptide and the natural binding partner **stabilizes** the native state of the polypeptide. (I) is also useful for assisting the binding between a polypeptide and a natural binding partner of the polypeptide, which involves **stabilizing** a native state of the polypeptide, and exposing the **stabilized** polypeptide to the natural binding partner; and for assisting the binding between a polypeptide and a first molecule, in which the polypeptide exists in a native state and a denatured state, which involves providing a second **stabilizing** molecule capable of binding to a site which at least partially overlaps a functional site in the native state of the polypeptide, allowing the second **stabilizing** molecule to bind to the polypeptide to form a complex and thereby **stabilizing** the native state of the polypeptide, exposing the polypeptide and bound second **stabilizing** molecule complex to the first molecule, and allowing the first molecule to bind to the polypeptide, and thereby displacing the second **stabilizing** molecule. The functional site comprises or at least partially overlaps with a structural domain, a protein binding domain, a nucleic acid binding domain or an active site of an enzyme. The functional site is essential to the structure or activity, or both, of the polypeptide. The polypeptide comprises an oncogenic protein or a tumor suppressor protein such as **p53**. (I) is useful for treating a disease, or in the manufacture of a medicament for treating the disease, e.g. cancer. (I) is also useful for inducing the onset or progression of apoptosis in one or more cells. (I) is useful for preparing a medicament for inducing the onset or progression of apoptosis in one or more cells. (All claimed.)

ADVANTAGE - (I) does not bind to the denatured/inactive form of the polypeptide, thus preferentially **stabilizing** the active conformation. (I) is capable of increasing the relative concentration of a native form of the polypeptide as compared to the a denatured form. Dwg.0/10

L12 ANSWER 5 OF 24 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 2003292121 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12700230
TITLE: Kinetic instability of **p53** core domain mutants: implications for rescue by small molecules.
AUTHOR: Friedler Assaf; Veprintsev Dmitry B; Hansson Lars O; Fersht Alan R
CORPORATE SOURCE: Cambridge University Chemical Laboratory and Cambridge Centre for Protein Engineering, Medical Research Council Centre, Hills Road, Cambridge CB2 2QH, United Kingdom.
SOURCE: Journal of biological chemistry, (2003 Jun 27) 278 (26) 24108-12. Electronic Publication: 2003-04-16. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 20030624
Last Updated on STN: 20030821
Entered Medline: 20030820

Searcher : Shears 571-272-2528

AB Oncogenic mutations in the tumor suppressor protein **p53** are found mainly in its DNA-binding core domain. Many of these mutants are thermodynamically unstable at body temperature. Here we show that these mutants also denature within minutes at 37 degrees C. The half-life (t(1/2)) of the unfolding of wild-type **p53** core domain was 9 min. Hot spot mutants denatured more rapidly with increasing thermodynamic instability. The highly destabilized **mutant I195T** had a t(1/2) of less than 1 min. The wild-type **p53** -(94-360) construct, containing the core and tetramerization domains, was more **stable**, with t(1/2) = 37 min at 37 degrees C, similar to full-length **p53**. After unfolding, the denatured proteins aggregated, the rate increasing with higher concentrations of protein. A derivative of the **p53-stabilizing** peptide CDB3 significantly slowed down the unfolding rate of the **p53** core domain. Drugs such as CDB3, which rescue the conformation of unstable mutants of **p53**, have to act during or immediately after biosynthesis. They should maintain the mutant protein in a folded conformation and prevent its aggregation, allowing it enough time to reach the nucleus and bind its sequence-specific target DNA or the **p53** binding proteins that will **stabilize** it.

L12 ANSWER 6 OF 24 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2003585060 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14634213
TITLE: **P53** hot-spot mutants are resistant to ubiquitin-independent degradation by increased binding to NAD(P)H:quinone oxidoreductase 1.
AUTHOR: Asher Gad; Lotem Joseph; Tsvetkov Peter; Reiss Veronica; Sachs Leo; Shaul Yosef
CORPORATE SOURCE: Department of Molecular Genetics, Weizmann Institute of Science, Rehovot 76100, Israel.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2003 Dec 9) 100 (25) 15065-70. Electronic Publication: 2003-11-21. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 20031216
Last Updated on STN: 20040124
Entered Medline: 20040123

AB Proteasomal degradation of **p53** is mediated by two alternative pathways that are either dependent or independent of both Mdm2 and ubiquitin. The ubiquitin-independent pathway is regulated by NAD(P)H: quinone oxidoreductase 1 (NQO1) that **stabilizes p53**. The NQO1 inhibitor dicoumarol induces ubiquitin-independent **p53** degradation. We now show that, like dicoumarol, several other coumarin and flavone inhibitors of NQO1 activity, which compete with NAD(P)H for binding to NQO1, induced ubiquitin-independent **p53** degradation and inhibited wild-type **p53**-mediated apoptosis. Although wild-type **p53** and several **p53 mutants** were sensitive to dicoumarol-induced degradation, the most frequent "hot-spot" **p53 mutants** in human cancer, **R175H**, R248H, and **R273H**, were resistant to dicoumarol-induced degradation, but

remained sensitive to Mdm2-ubiquitin-mediated degradation. The two alternative pathways for **p53** degradation thus have different **p53** structural requirements. Further mutational analysis showed that arginines at positions 175 and 248 were essential for dicoumarol-induced **p53** degradation. NQO1 bound to wild-type **p53** and dicoumarol, which induced a conformational change in NQO1, inhibited this binding. Compared with wild-type **p53**, the hot-spot **p53** mutants showed increased binding to NQO1, which can explain their resistance to dicoumarol-induced degradation. NQO1 thus has an important role in **stabilizing** hot-spot **p53** mutant proteins in human cancer.

L12 ANSWER 7 OF 24 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2003089069 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12600206
TITLE: Structure, function, and aggregation of the zinc-free form of the **p53** DNA binding domain.
AUTHOR: Butler James S; Loh Stewart N
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, State University of New York Upstate Medical University, 750 East Adams Street, Syracuse, New York 13210, USA.
SOURCE: Biochemistry, (2003 Mar 4) 42 (8) 2396-403.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 20030226
Last Updated on STN: 20030529
Entered Medline: 20030528

AB The **p53** DNA binding domain (DBD) contains a single bound zinc ion that is essential for activity. Zinc remains bound to wild-type DBD at temperatures below 30 degrees C; however, it rapidly dissociates at physiological temperature. The resulting zinc-free protein (apoDBD) is folded and **stable**. NMR spectra reveal that the DNA binding surface is altered in the absence of Zn(2+). Fluorescence anisotropy studies show that Zn(2+) removal abolishes site-specific DNA binding activity, although full nonspecific DNA binding affinity is retained. Surprisingly, the majority of tumorigenic mutations that destabilize DBD do not appreciably destabilize apoDBD. The **R175H mutation** instead substantially accelerates the rate of Zn(2+) loss. A considerable fraction of cellular **p53** may therefore exist in the folded zinc-free form, especially when tumorigenic mutations are present. ApoDBD appears to promote aggregation of zinc-bound DBD via a nucleation-growth process. These data provide an explanation for the dominant negative phenotype exhibited by many mutations. Through a combination of induced **p53** aggregation and diminished site-specific DNA binding activity, Zn(2+) loss may represent a significant inactivation pathway for **p53** in the cell.

L12 ANSWER 8 OF 24 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2003468465 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14529628
TITLE: Conversion of wild-type **p53** core domain into a conformation that mimics a hot-spot mutant.

AUTHOR: Ishimaru Daniella; Maia Lenize F; Maiolino Larissa M; Quesado Pablo A; Lopez Priscila C M; Almeida Fabio C L; Valente Ana Paula; Silva Jerson L
CORPORATE SOURCE: Departamento de Bioquimica Medica, Centro Nacional de Ressonancia Magnetica Nuclear de Macromoleculas, Instituto de Ciencias Biomedicas, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ 21941-590, Brazil.
SOURCE: Journal of molecular biology, (2003 Oct 17) 333 (2) 443-51. Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 20031008
Last Updated on STN: 20031111
Entered Medline: 20031110

AB The wild-type **p53** protein can be driven into a conformation corresponding to that adopted by structural mutant forms by heterodimerization with a mutant subunit. To seek partially folded states of the wild-type **p53** core domain (p53C) we used high hydrostatic pressure (HP) and subzero temperatures. Aggregation of the protein was observed in parallel with its pressure denaturation at 25 and 37 degrees C. However, when HP experiments were performed at 4 degrees C, the extent of denaturation and aggregation was significantly less pronounced. On the other hand, subzero temperatures under pressure led to cold denaturation and yielded a non-aggregated, alternative conformation of p53C. Nuclear magnetic resonance (1H15N-NMR) data showed that the alternative p53C conformation resembled that of the hot-spot oncogenic **mutant R248Q**. This alternative state was as susceptible to denaturation and aggregation as the **mutant R248Q** when subjected to HP at 25 degrees C. Together these data demonstrate that wild-type p53C adopts an alternative conformation with a mutant-like **stability**, consistent with the dominant-negative effect caused by many mutants. This alternative conformation is likely related to inactive forms that appear in vivo, usually driven by interaction with mutant proteins. Therefore, it can be a valuable target in the search for ways to interfere with protein misfolding and hence to prevent tumor development.

L12 ANSWER 9 OF 24 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2003509914 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14587098
TITLE: Elevated levels of prostate-specific antigen (PSA) in prostate cancer cells expressing mutant **p53** is associated with tumor metastasis.
AUTHOR: Downing Sean; Bumak Clare; Nixdorf Sheri; Ow Kim; Russell Pamela; Jackson Paul
CORPORATE SOURCE: Oncology Research Centre, Prince of Wales Hospital, Randwick, NSW, Australia.
SOURCE: Molecular carcinogenesis, (2003 Nov) 38 (3) 130-40. Journal code: 8811105. ISSN: 0899-1987.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312

ENTRY DATE: Entered STN: 20031031
Last Updated on STN: 20031219
Entered Medline: 20031212

AB The underlying basis for rising levels of prostate-specific antigen (PSA) in prostate cancer is not fully understood, but attention has turned to the possibility that loss of normal **p53** function might be directly involved. We have investigated the relationship between **p53** function and PSA expression using in vitro and in vivo approaches. Three prostate cancer-derived **p53 mutants** (F134L, M237L, **R273H**) were introduced into LNCaP prostate cancer cells and **stable** transfectants established. Expression of mutant **p53** was demonstrated by Western blot analysis, inactivation of wtp53 function, and a loss of **p53**-dependent responses to DNA damage induced by UV-irradiation and cisplatin. Levels of PSA mRNA and secreted protein were determined by RT-PCR and Western blotting, respectively. Serine protease activity was assessed using an esterase assay. In vivo effects of mutant **p53** expression were examined after orthotopic implantation into prostates of nude mice. Expression of all **p53** mutants was associated with elevated PSA mRNA and secreted PSA protein. In a representative line, mutant **p53** was also associated with increased PSA protease-like activity compared with a control line expressing wildtype **p53**. Overall PSA levels, and PSA levels in serum from mice bearing tumors derived from cells expressing mutant **p53**, were increased compared with levels in mice bearing tumors derived from control cells. In addition, the tumors derived from cells with mutant **p53** had increased vascularization and induced lymph node metastases. These data provide in vitro and in vivo support for the notion that **p53** mutations directly contribute to increased levels of serum PSA, and are associated with more aggressive tumors.

L12 ANSWER 10 OF 24 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2002210482 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11948395
TITLE: Characterization of the **p53**-rescue drug CP-31398 in vitro and in living cells.
AUTHOR: Rippin Thomas M; Bykov Vladimir J N; Freund Stefan M V; Selivanova Galina; Wiman Klas G; Fersht Alan R
CORPORATE SOURCE: Cambridge University Chemical Laboratory and Cambridge Center for Protein Engineering, MRC Centre, Hills Road, Cambridge CB2 2QH, UK.
SOURCE: Oncogene, (2002 Mar 28) 21 (14) 2119-29.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020412
Last Updated on STN: 20020501
Entered Medline: 20020430

AB The Pfizer compound CP-31398 has been reported to **stabilize** the core domain of the tumour suppressor **p53** in vitro and be an effective anti-cancer drug by virtue of rescuing destabilized mutants of **p53**. We did not detect any interaction between the **p53**

core domain and CP-31398 in vitro by a wide range of quantitative biophysical techniques over a wide range of conditions. CP-31398 did not **stabilize p53** in our experiments. However, we found that CP-31398 intercalated with DNA and also altered and destabilized the DNA-**p53** core domain complex. We analysed by NMR TROSY the interaction of the domain with a DNA oligomer and identified the changes in the complex on the binding of CP-31398. CP-31398 also decreased sequence-specific DNA binding of wild-type **p53** and His-273 mutant **p53**. CP-31398 had a non-specific toxic effect independent of mutant **p53** expression in several cell lines carrying Tet-regulated mutant **p53**. CP-31398 caused a small increase in MDM-2 expression and a more pronounced **p53** -independent increase in Bax expression. CP-31398 did, however, induce the PAb1620 epitope (characteristic of native **p53**) in cells expressing His-175 mutant **p53**. This was prevented by cycloheximide, suggesting that any **stabilizing** action of CP-31398 would have to be on newly synthesized **p53**. One of the unstable **mutants** that was reported to have been rescued by CP-31398, **R249S**, does not bind DNA when folded at lower temperatures.

L12 ANSWER 11 OF 24 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2002175455 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11782540
TITLE: A peptide that binds and **stabilizes p53** core domain: chaperone strategy for rescue of oncogenic mutants.
AUTHOR: Friedler Assaf; Hansson Lars O; Veprintsev Dmitry B; Freund Stefan M V; Rippin Thomas M; Nikolova Penka V; Proctor Mark R; Rudiger Stefan; Fersht Alan R
CORPORATE SOURCE: Cambridge University Chemical Laboratory and Cambridge Centre for Protein Engineering, Medical Research Council Centre, Hills Road, Cambridge CB2 2QH, United Kingdom.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2002 Jan 22) 99 (2) 937-42. Electronic Publication: 2002-01-08. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020324
Last Updated on STN: 20030105
Entered Medline: 20020429

AB Conformationally compromised oncogenic mutants of the tumor suppressor protein **p53** can, in principle, be rescued by small molecules that bind the native, but not the denatured state. We describe a strategy for the rational search for such molecules. A nine-residue peptide, CDB3, which was derived from a **p53** binding protein, binds to **p53** core domain and **stabilizes** it in vitro. NMR studies showed that CDB3 bound to **p53** at the edge of the DNA binding site, partly overlapping it. The fluorescein-labeled peptide, FL-CDB3, binds wild-type **p53** core domain with a dissociation constant of 0.5 microM, and raises the apparent melting temperatures of wild-type and a representative oncogenic **mutant, R249S** core domain.

gadd45 DNA competes with CDB3 and displaces it from its binding site. But this competition does not preclude CDB3 from being a lead compound. CDB3 may act as a "chaperone" that maintains existing or newly synthesized destabilized **p53** mutants in a native conformation and then allows transfer to specific DNA, which binds more tightly. Indeed, CDB3 restored specific DNA binding activity to a highly destabilized **mutant I195T** to close to that of wild-type level.

L12 ANSWER 12 OF 24 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2001352168 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11416144
TITLE: ZBP-89 promotes growth arrest through **stabilization** of **p53**.
AUTHOR: Bai L; Merchant J L
CORPORATE SOURCE: Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, USA.
CONTRACT NUMBER: 5P30 CA46592-13 (NCI)
DK 55732 (NIDDK)
SOURCE: Molecular and cellular biology, (2001 Jul) 21 (14) 4670-83. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010730
Last Updated on STN: 20010730
Entered Medline: 20010726

AB Transcription factor **p53** can induce growth arrest and/or apoptosis in cells through activation or repression of downstream target genes. Recently, we reported that ZBP-89 cooperates with histone acetyltransferase coactivator p300 in the regulation of p21(waf1), a cyclin-dependent kinase inhibitor whose associated gene is a target gene of **p53**. Therefore, we examined whether ZBP-89 might also inhibit cell growth by activating **p53**. In the present study, we demonstrate that elevated levels of ZBP-89 induce growth arrest and apoptosis in human gastrointestinal cell lines. The ZBP-89 protein accumulated within 4 h, and the **p53** protein accumulated within 16 h, of serum starvation without changes in p14ARF levels, demonstrating a physiological increase in the cellular levels of these two proteins. Overexpression of ZBP-89 **stabilized** the **p53** protein and enhanced its transcriptional activity through direct protein-protein interactions. The DNA binding and C-terminal domains of **p53** and the zinc finger domain of ZBP-89 mediated the interaction. A point **mutation** in the **p53** DNA binding domain, **R273H**, greatly reduced ZBP-89-mediated **stabilization** but not their physical interaction. Furthermore, ZBP-89 formed a complex with **p53** and MDM2 and therefore did not prevent the MDM2-**p53** interaction. However, heterokaryon assays demonstrated that ZBP-89 retained **p53** in the nucleus. Collectively, these data indicate that ZBP-89 regulates cell proliferation in part through its ability to directly bind the **p53** protein and retard its nuclear export. Our findings further our understanding of how ZBP-89 modulates cell proliferation and reveals a novel mechanism by which the **p53** protein is **stabilized**.

L12 ANSWER 13 OF 24 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2001214517 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11172034
TITLE: **p53** associates with and targets Delta Np63 into a protein degradation pathway.
AUTHOR: Ratovitski E A; Patturajan M; Hibi K; Trink B; Yamaguchi K; Sidransky D
CORPORATE SOURCE: Department of Otolaryngology-Head and Neck Surgery, Division of Head and Neck Cancer Research, The Johns Hopkins University School of Medicine, Baltimore, MD 21205-2196, USA.. erat@welch.jhu.edu
CONTRACT NUMBER: CA-58184-01 (NCI)
R01-AI-47224-01 (NIAID)
R01-DE-012588-01 (NIDCR)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2001 Feb 13) 98 (4) 1817-22. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010425
Last Updated on STN: 20010425
Entered Medline: 20010419

AB A human **p53** homologue, p63 (p40/p51/p73L/CUSP) that maps to the chromosomal region 3q27-29 was found to produce a variety of transcripts that encode DNA-binding proteins with and without a trans-activation domain (TA- or Delta N-, respectively). The p63 gene locus was found to be amplified in squamous cell carcinoma, and overexpression of Delta Np63 (p40) led to increased growth of transformed cells in vitro and in vivo. Moreover, p63-null mice displayed abnormal epithelial development and germ-line human mutations were found to cause ectodermal dysplasia. We now demonstrate that certain p63 isotypes form complexes with **p53** . **p53 mutations R175H** or R248W abolish the association of **p53** with p63, whereas V143A or **R273H** has no effect. Deletion studies suggest that the DNA-binding domains of both **p53** and p63 mediate the association. Overexpression of wild type but not **mutant** (**R175H**) **p53** results in the caspase-dependent degradation of certain Delta Np63 proteins (p40 and Delta Np63 alpha). The association between **p53** and Delta Np63 supports a previously unrecognized role for **p53** in regulation of Delta Np63 **stability**. The ability of **p53** to mediate Delta Np63 degradation may balance the capacity of Delta Np63 to accelerate tumorigenesis or to induce epithelial proliferation.

L12 ANSWER 14 OF 24 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2001244234 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11314010
TITLE: p73 is transcriptionally regulated by DNA damage, **p53**, and p73.
AUTHOR: Chen X; Zheng Y; Zhu J; Jiang J; Wang J
CORPORATE SOURCE: Institute of Molecular Medicine and Genetics, Medical College of Georgia, Augusta, GA 30912, USA.
CONTRACT NUMBER: CA76069 (NCI)
RO1 CA81237 (NCI)

SOURCE: Oncogene, (2001 Feb 8) 20 (6) 769-74.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010510

AB p73 is a member of the **p53** family. Recent studies have shown that DNA damage can **stabilize** p73 protein and enhance p73-mediated apoptosis in a c-Abl dependent manner. To determine what regulates p73 transcriptionally, we analysed the expression of p73 in several cell lines following genotoxic stresses. We found that p73 is induced in certain cell lines when treated with therapeutic DNA damaging agents. We also found that **p53** and p73, but not **mutant p53(R249S)** and p73beta292, directly induce the expression of the p73 gene. In addition, we found one potential **p53**-binding site in the promoter of the p73 gene. This binding site is responsive to **p53**, p73, and DNA damage. Taken together, these data suggest that p73 is transcriptionally regulated by DNA damage and **p53**, and is autoregulated.

L12 ANSWER 15 OF 24 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 2001377498 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11435891
TITLE: Various forms of mutant **p53** confer sensitivity to cisplatin and doxorubicin in bladder cancer cells.
AUTHOR: Chang F L; Lai M D
CORPORATE SOURCE: Department of Biochemistry, College of Medicine, National Cheng Kung University, Tainan, Taiwan, Republic of China.
SOURCE: Journal of urology, (2001 Jul) 166 (1) 304-10.
Journal code: 0376374. ISSN: 0022-5347.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20010813
Entered Medline: 20010809

AB PURPOSES: The nature of **p53** mutation has been reported to affect cellular responses to chemotherapy. We characterized the impact of **p53** mutations on drug resistance in bladder cancer cells. METHODS AND METHODS: Various human **p53 mutants** (V143A, V173L, H179Q, N247I and **R273H**) were introduced to the TCC-SUP bladder carcinoma cell line to establish **stable** transfectants. The expression of mutant **p53** was demonstrated by reverse transcriptase-polymerase chain reaction and immunocytochemical analysis. The sensitivity to cisplatin and doxorubicin in these transfectants was determined by trypan blue exclusion. Cell death mediated by cisplatin and doxorubicin was characterized by terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick end-labeling analysis, Hoechst 33258 staining and annexin-V binding assay. RESULTS: The expression of all forms of mutant **p53** protein except p53His273

enhanced sensitivity to cisplatin and doxorubicin. The chemosensitivity of p53His273 transfectants is similar to that of parental TCC-SUP and control transfectants. Cisplatin induced cell death undergoes apoptosis, as demonstrated by Hoechst staining, annexin-V assay and terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick end-labeling, respectively. In contrast, doxorubicin induced cell death probably occurs through a nonapoptotic pathway. CONCLUSIONS: These results indicated that the nature of **p53** mutations may affect the cellular response to anticancer drugs and many forms of mutant **p53** protein may enhance chemosensitivity through apoptotic or nonapoptotic pathways in bladder cancer cells.

L12 ANSWER 16 OF 24 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 14

ACCESSION NUMBER: 2000:166344 BIOSIS
DOCUMENT NUMBER: PREV200000166344
TITLE: Quantitative analysis of residual folding and DNA binding in mutant **p53** core domain: Definition of mutant states for rescue in cancer therapy.
AUTHOR(S): Bullock, Alex N.; Henckel, Julia; Fersht, Alan R. [Reprint author]
CORPORATE SOURCE: Cambridge University Chemical Laboratory and Cambridge Centre for Protein Engineering, Medical Research Council Centre, Hills Road, Cambridge, CB2 2QH, UK
SOURCE: Oncogene, (March 2, 2000) Vol. 19, No. 10, pp. 1245-1256. print.
CODEN: ONCNES. ISSN: 0950-9232.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 3 May 2000
Last Updated on STN: 4 Jan 2002

AB The tumour suppressor **p53** is mutated in half of all human cancers, most frequently with missense substitutions in its core domain. We present a new assessment of the mutation database based on quantitative folding and DNA-binding studies of the isolated core domain. Our data identify five distinct mutant classes that correlate with four well-defined regions of the core domain structure. On extrapolation to 37degreeC the wild-type protein has a **stability** of 3.0 kcal/mol. This also emerges as an oncogenic threshold: all beta-sandwich mutants destabilized by this amount (50% denatured) are expected to promote cancer. Other weakly destabilizing mutations are restricted to loop 3 in the DNA-binding region. Drugs that **stabilize** mutant **p53** folding have the potential to reactivate apoptotic signalling pathways in tumour cells either by transactivation-dependent or independent pathways. Using an affinity ligand as a proof of principle we have recovered the thermodynamic **stability** of the hotspot G245S. With reference states for the five mutant classes as a guide, future therapeutic strategies may similarly **stabilize** partially structured or binding states of mutant **p53** that restore limited **p53** pathways to tumour suppression.

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ACCESSION NUMBER: 2000:478769 BIOSIS
DOCUMENT NUMBER: PREV200000478769
TITLE: **Stability** studies of **p53** tumour

suppressor mutants.
AUTHOR(S): Nikolova, Penka V. [Reprint author]; Wong, Kam-Bo [Reprint author]; Dedecker, Brian [Reprint author]; Henckel, Julia [Reprint author]; Fersht, Alan R. [Reprint author]
CORPORATE SOURCE: MRC Centre, Cambridge University Chemical Laboratory and Cambridge Centre for Protein Engineering, Hills Road, Cambridge, CB2 2QH, UK
SOURCE: Journal of Biomolecular Structure and Dynamics, (June, 2000) Vol. 17, No. 6, pp. 1149-1150. print.
Meeting Info.: Conference on DNA Structure and Interactions: Their Biological Roles and Implications in Biomedicine and Biotechnologies. Brno, Czech Republic. July 19-23, 2000.
CODEN: JBSDD6. ISSN: 0739-1102.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Nov 2000
Last Updated on STN: 10 Jan 2002

L12 ANSWER 18 OF 24 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 2000120801 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10654936
TITLE: Mechanism of rescue of common **p53** cancer mutations by second-site suppressor mutations.
AUTHOR: Nikolova P V; Wong K B; DeDecker B; Henckel J; Fersht A R
CORPORATE SOURCE: Cambridge University Chemical Laboratory and Cambridge Centre for Protein Engineering, MRC Centre, Hills Road, Cambridge CB2 2QH, UK.
SOURCE: EMBO journal, (2000 Feb 1) 19 (3) 370-8.
Journal code: 8208664. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000327
Last Updated on STN: 20000327
Entered Medline: 20000310

AB The core domain of **p53** is extremely susceptible to mutations that lead to loss of function. We analysed the **stability** and DNA-binding activity of such mutants to understand the mechanism of second-site suppressor mutations. Double-**mutant** cycles show that N239Y and N268D act as 'global **stability**' suppressors by increasing the **stability** of the cancer **mutants** **G245S** and V143A-the free energy changes are additive. Conversely, the suppressor H168R is specific for the **R249S mutation** : despite destabilizing wild type, H168R has virtually no effect on the **stability** of **R249S**, but restores its binding affinity for the gadd45 promoter. NMR structural comparisons of R249S/H168R and R249S/T123A/H168R with wild type and R249S show that H168R reverts some of the structural changes induced by R249S. These results have implications for possible drug therapy to restore the function of tumorigenic **mutants** of **p53**: the function of **mutants** such as V143A and **G245S** is theoretically possible to restore by small molecules that simply bind to and hence **stabilize** the native

structure, whereas **R249S** requires alteration of its **mutant** native structure.

L12 ANSWER 19 OF 24 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 1999243189 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10226602
TITLE: Modulation of wild-type **p53** activity by **mutant p53 R273H** depends on the **p53** responsive element (p53RE). A comparative study between the p53REs of the MDM2, WAFI/Cip1 and Bax genes in the lung cancer environment. WAFI/Cip1 = WAF1/Cip1.
AUTHOR: Zacharatos P V; Gorgoulis V G; Kotsinas A; Manolis E N; Liloglou T; Rassidakis A N; Kanavaros P; Field J D; Halazonetis T; Kittas C
CORPORATE SOURCE: Department of Histology and Embryology, School of Medicine, University of Athens, Greece.
SOURCE: Anticancer research, (1999 Jan-Feb) 19 (1A) 579-87. Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990601
Last Updated on STN: 19990601
Entered Medline: 19990520

AB Wild-type (wt) **p53** is a tumor-suppressor protein which acts via transcriptional and transcriptional-independent mechanisms. The transcriptional function of **p53** is mediated by specific responsive elements (REs). The MDM2, WAF1/Cip1 and Bax genes possess p53REs and their activation by wt **p53** induces cell cycle progression, arrest and programmed cell death (apoptosis), respectively. Mutations of the **p53** gene are detected in more than 50% of the human malignant tumors. **p53** mutants seem to have a more **stable** conformation and are suggested to exert dominant-negative inhibition of wt **p53** in cells containing both wt and mutant (mt) alleles. However, recent studies show that certain mt **p53** proteins posses a "gain of function" phenotype. In the present study, we examined the effects of the second most frequent **p53** **mutant R273H** on the p53REs of the MDM2, WAF1/Cip1 and Bax genes in the H1299 non-small cell lung carcinoma cell line. Although mt **p53** R273H alone was unable to bind and transactivate the corresponding p53REs, it enhanced the MDM2-p53RE mediated gene transcription of wt **p53** (positive-dominant effect) and prevented the wt **p53** transactivation of the p53REs of WAF1/Cip1 and Bax genes (negative-dominant effect). Our data suggest that in the appropriate environment, differential transcription of critical **p53** target genes by certain **p53** mutant proteins may illustrate another mechanism implicated in tumor development.

L12 ANSWER 20 OF 24 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 1998216785 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9557707
TITLE: Adenovirus type 12-induced fragility of the human RNU2 locus requires **p53** function.
AUTHOR: Li Z; Yu A; Weiner A M

Searcher : Shears 571-272-2528

CORPORATE SOURCE: Department of Molecular Biophysics and Biochemistry, Yale University, New Haven, Connecticut 06520-8114, USA.
CONTRACT NUMBER: GM31073 (NIGMS)
GM41624 (NIGMS)
SOURCE: Journal of virology, (1998 May) 72 (5) 4183-91.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980529
Last Updated on STN: 19990129
Entered Medline: 19980520

AB Adenovirus type 12 (Ad12) infection of human cells induces four chromosomal fragile sites corresponding to the U1 small nuclear RNA (snRNA) genes (the RNU1 locus), the U2 snRNA genes (RNU2), the U1 snRNA pseudogenes (PSU1), and the 5S rRNA genes (RN5S). Ad12-induced fragility of the RNU2 locus requires U2 snRNA transcriptional regulatory elements and viral early functions but not viral replication or integration, or chromosomal sequences flanking the RNU2 locus. We now show that Ad12 cannot induce the RNU1, RNU2, or PSU1 fragile sites in Saos-2 cells lacking the **p53** and retinoblastoma (Rb) proteins but that viral induction of fragility is rescued in these cells when the expression of wild-type **p53** or selected hot-spot **mutants** (i.e., V143A, **R175H**, R248W, and **R273H**) is restored by transient expression or **stable** retroviral transduction. We also observed weak constitutive fragility of the RNU1 and RNU2 loci in cells belonging to xeroderma pigmentosum complementation groups B and D (XPB and XPD) which are partially defective in the ERCC2 (XPD) and ERCC3 (XPB) helicase activities shared between the repairosome and the RNA polymerase H basal transcription factor TFIIH. We propose a model for Ad12-induced chromosome fragility in which interaction of **p53** with the Ad12 E1B 55-kDa transforming protein (and possibly E4orf6) induces a **p53** gain of function which ultimately perturbs the RNA polymerase II basal transcription apparatus. The **p53** gain of function could interfere with chromatin condensation either by blocking mitotic shutdown of U1 and U2 snRNA transcription or by phenocopying global or local DNA damage. Specific fragilization of the RNU1, RNU2, and PSU1 loci could reflect the unusually high local concentration of strong transcription units or the specialized nature of the U1 and U2 snRNA transcription apparatus.

L12 ANSWER 21 OF 24 MEDLINE on STN DUPLICATE 18

ACCESSION NUMBER: 1998190068 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9524109
TITLE: Genetic selection of intragenic suppressor mutations that reverse the effect of common **p53** cancer mutations.
AUTHOR: Brachmann R K; Yu K; Eby Y; Pavletich N P; Boeke J D
CORPORATE SOURCE: Department of Molecular Biology and Genetics, The Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA.
CONTRACT NUMBER: CA 16519 (NCI)
SOURCE: EMBO journal, (1998 Apr 1) 17 (7) 1847-59.
Journal code: 8208664. ISSN: 0261-4189.

PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980611
Last Updated on STN: 19980611
Entered Medline: 19980601

AB Several lines of evidence suggest that the presence of the wild-type tumor suppressor gene **p53** in human cancers correlates well with successful anti-cancer therapy. Restoration of wild-type **p53** function to cancer cells that have lost it might therefore improve treatment outcomes. Using a systematic yeast genetic approach, we selected second-site suppressor mutations that can overcome the deleterious effects of common **p53** cancer mutations in human cells. We identified several suppressor **mutations** for the V143A, **G245S** and **R249S** cancer **mutations**. The beneficial effects of these suppressor mutations were demonstrated using mammalian reporter gene and apoptosis assays. Further experiments showed that these suppressor mutations could override additional **p53** cancer mutations. The mechanisms of such suppressor mutations can be elucidated by structural studies, ultimately leading to a framework for the discovery of small molecules able to **stabilize** **p53** mutants.

L12 ANSWER 22 OF 24 MEDLINE on STN DUPLICATE 19
ACCESSION NUMBER: 1998070752 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9405613
TITLE: Thermodynamic **stability** of wild-type and mutant **p53** core domain.
AUTHOR: Bullock A N; Henckel J; DeDecker B S; Johnson C M; Nikolova P V; Proctor M R; Lane D P; Fersht A R
CORPORATE SOURCE: Cambridge University Chemical Laboratory and Cambridge Centre for Protein Engineering, Medical Research Council Centre, Hills Road, Cambridge CB2 2QH, United Kingdom.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1997 Dec 23) 94 (26) 14338-42. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980217
Last Updated on STN: 19980217
Entered Medline: 19980202

AB Some 50% of human cancers are associated with mutations in the core domain of the tumor suppressor **p53**. Many mutations are thought just to destabilize the protein. To assess this and the possibility of rescue, we have set up a system to analyze the **stability** of the core domain and its mutants. The use of differential scanning calorimetry or spectroscopy to measure its melting temperature leads to irreversible denaturation and aggregation and so is useful as only a qualitative guide to **stability**. There are excellent two-state denaturation curves on the addition of urea that may be analyzed quantitatively. One Zn2+ ion remains tightly bound in the holo-form of **p53** throughout the

denaturation curve. The **stability** of wild type is 6.0 kcal (1 kcal = 4.18 kJ)/mol at 25 degrees C and 9.8 kcal/mol at 10 degrees C. The oncogenic **mutants R175H**, C242S, **R248Q**, **R249S**, and **R273H** are destabilized by 3.0, 2.9, 1.9, 1.9, and 0.4 kcal/mol, respectively. Under certain denaturing conditions, the wild-type domain forms an aggregate that is relatively highly fluorescent at 340 nm on excitation at 280 nm. The destabilized mutants give this fluorescence under milder denaturation conditions.

L12 ANSWER 23 OF 24 CANCERLIT on STN
ACCESSION NUMBER: 97618953 CANCERLIT
DOCUMENT NUMBER: 97618953
TITLE: Doxorubicin induces G2/M arrest and apoptosis in the **p53** mutant cell line HT-29 (Meeting abstract).
AUTHOR: Giacona M; Brown T; Giedlin M; Yamamoto R
CORPORATE SOURCE: CHIRON Corp. Dept of Pharmacology, BioPharmaceutical Evaluation, Emeryville, CA 94608.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, (1997) 38 A131. ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
LANGUAGE: English
FILE SEGMENT: Institute for Cell and Developmental Biology
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19980417
Last Updated on STN: 19980417

AB Normal cells are thought to acquire a cancerous phenotype through a process involving multiple genetic changes. The nuclear phosphoprotein **p53** is a tumor suppressor that functions to maintain genomic **stability** in cells by inducing growth arrest or apoptosis. Cells with **mutations** that result in altered or non-functional **p53** protein are highly selected for during cancer progression. Most if not all chemotherapeutics kill tumor cells by triggering apoptosis. To better understand the mechanisms behind cancer chemotherapeutics in a **p53 mutant** background a human colon adenocarcinoma cell line HT-29 (**R273H**) was used as a model system. Doxorubicin induced the gene expression of p21waf1/cip1 a cyclin-dependent kinase inhibitor within 3 hours of exposure. Flow cytometry analysis of propidium iodide and FITC-dUTP stained cells showed growth arrest and apoptosis at G2/M. As a biochemical indicator of apoptosis the fluorescent substrate DEVD-AFC was used to monitor the appearance of apoptosis-associated cysteine protease activity in doxorubicin-treated cells. Enzyme activity in HT29 cells was detected at 48 hrs and in HCT116 cells at 24 hrs. The relative potencies of several clinically relevant chemotherapeutics were rank ordered by this enzyme assay: (Doxorubicin=Camptothecin greater than Paclitaxel=Etoposide). Insights into the cell cycle checkpoints and apoptosis in normal vs cancer cells provides a useful framework for identifying new agents for antineoplastic therapy and alternative uses for conventional chemotherapeutics.

L12 ANSWER 24 OF 24 CANCERLIT on STN
ACCESSION NUMBER: 96601077 CANCERLIT
DOCUMENT NUMBER: 96601077
TITLE: Use of temperature-sensitive (TS) mutants of the v-Rel oncoprotein to study apoptosis in chicken spleen cells (Meeting abstract).

AUTHOR: White D; Gilmore T
CORPORATE SOURCE: Biology Department, Boston University, Boston, MA 02215.
SOURCE: J Cell Biochem, (1995) Suppl 19A 64.
ISSN: 0730-2312.
DOCUMENT TYPE: (MEETING ABSTRACTS)
LANGUAGE: English
FILE SEGMENT: Institute for Cell and Developmental Biology
ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 19970509
Last Updated on STN: 19970509

AB The v-Rel nuclear oncoprotein is a transcription factor encoded by the avian Rev-T retrovirus that can transform and immortalize chicken spleen cells in vitro. We have constructed two ts v-Rel **mutants** (v-**R273H** and v-G37E) that are ts for transformation and DNA binding. When ts v-Rel-transformed chicken spleen cells are shifted to the nonpermissive temperature, the cells rapidly undergo apoptosis, as characterized by condensed chromatin and the formation of 'DNA ladders.' Many proteins, including v-Rel, Bcl-2, c-Myc, Rb and **p53**, are quite **stable** in these cells while undergoing apoptosis. However, the v-Rel-associated protein p40 (I kappa B-alpha) is specifically degraded when ts v-Rel-transformed cells are shifted to the nonpermissive temperature. In cells transformed by ts v-Rel **mutant** v-**R273H**, p40 is completely degraded, similar to what is observed in other cells in which Rel complexes are induced to enter the nucleus. In cells transformed by ts v-Rel **mutant** v-G37E, p40 is cleaved to an intermediate form, which is found in a detergent-insoluble fraction and is missing approximately 3 kD from the N terminus. These results suggest that v-Rel **stabilizes** p40 in transformed cells and that changes in the structure of a Rel/NF-kappa B protein can initiate proteolysis of an associated I kappa B protein. Furthermore, they indicate that v-Rel blocks a normal pathway of programmed cell death as part of its transforming and immortalizing process. We are currently attempting to understand the molecular basis for v-Rel-mediated inhibition of apoptosis.

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